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CLAUDE BERNARD ISSUE

October, 1949

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GUEST EDITORIAL

Medical Care in England

MUCH of the English-speaking world is observing attentively the sweeping experiments in Great Britain in which agencies of the central government are undertaking vastly increased responsibilities for the economic well-being and physical welfare of the whole people. One of the most popular of these measures appears to be the Act which instituted the British National Health Service.

To a number of publications in our American lay periodicals attesting to the enthusiasm of the potential British consumer for this service, I can add the results of a tiny poll which I took myself. In a series of follow-up letters early this year to two groups of former patients on whom I operated during four years of practice in Great Britain, there was appended to the specific clinical questions a request for an opinion of the new health service. In the great majority of the replies the scheme was praised to the skies. And approbation of this system of medical care does not come alone from the lowly. No less an apostle of individual freedom than the Right Honourable Mr. Winston Churchhill spoke with pride at the Massachusetts Institute of Technology recently on the part he had played as a member of the original Lloyd George Government in 1912 in initiating the prototype of the current scheme, the Panel System of those earlier years.

The opinions of the doctors who are expected to render the unlimited service provided by the Act, in return for a small fixed remuneration and aided by grossly limited facilities, form quite another story. As implied in an article published in February, my personal friends in the British medical profession were, to a man, agreed that additional major handicaps to proper treatment of ill patients had been interposed by the new legislation. The plethora of persons presenting minor complaints and requests has overburdened the general practitioners and this influx has deprived the seriously ill of the time with the doctor necessary for the recognition of that fact and for precise diagnosis. Although the cost of the medical provisions of the new legislation has vastly exceeded the original estimates, it is striking that the two major needs of British medicine: 1) increased numbers of trained consultants with more facilities for their work and 2) diagnostic and laboratory centers for general practitioners, have not been significantly touched by the program as yet. As long as the first of these deficiencies persists, patients who are obviously ill cannot get into hospitals to secure definitive treatment despite urgent pleas by the family physician to the appropriate consultant service. I have seen physicians devoting numerous phone calls over a period of weeks to the lone hospital in the region to which they might send a person with a brain tumour, describing the progressive deterioration of the patients, but failing to secure admission for lack of beds and personnel. It is small wonder that a doctor, after such disheartening experiences once he has made a diagnosis, may not trouble to try for any early diagnosis which might require therapy in a hospital.

The large number of patients to be seen by the doctor in the course of 24 hours—50 to 100 home and office cases per day is the current quota for many British physicians—

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means that he must find some graceful tactic for terminating within a few minutes the interview with every patient. By far the simplest means of coping with this problem of keeping the line moving is the dispensation of a prescription, which happily for the goodwill of the patient costs nothing to him directly. A vast increase in the British expenditure for drugs has in fact occurred. The anomalous situation now appears to exist in Great Britain in which the only ones who cannot secure at least vaguely appropriate medical attention are those who are really ill. While more votes can undoubtedly be purchased at less cost by providing people with medicinals and with dentures, one hopes that in time funds will be spared and arrangements made so that a reasonable proportion of the British medical profession can be utilised in the care of serious illness.

Although many physicians continue their work with unflagging zeal, the manifest exploitation of their goodwill and industry has reached an end in some cases. A British physician addressing a group in Boston recently ventured to cite instances in which some doctors who had put in long hours at their offices prior to the National Health Service Act, had gradually reduced their total hours of work, racing through a much larger number of talks with patients for a shorter working day than that to which they were wont before the new law went into effect.

Such an attitude represents the beginning of a vicious circle which, if unchecked, will soon lead to the catastrophic situation wherein the doctor and the community at large will have become enemies. A Scottish physician recently visiting at the Massachusetts General Hospital volunteered that she did not know a single member of the British medical profession who had not gone through what she described as at least one "acute depression" over his lot under the present system. The medical book representative of a prominent British publishing firm wrote recently to Mr. Charles C. Thomas that he had made a trip about his country to see "why people were not buying medical books". He found that "the medical profession is full of unrest, is decidedly poorer than it has ever been before . . . and just has not got the money to spare for books".

For the benefit of those who have arrived at a less bleak picture of the scene from casual British medical contacts, one may point out that this proud and capable folk eschew a public washing of their dirty linen. Hence those whose information comes from longstanding personal friends are perhaps more likely to reach a truer evaluation than those who conduct a series of journalistic interviews with the avowed purpose of writing up their data for publication. Our experience with British medical visitors over the past 9 months has, however, shown an increasing trend in them towards a more outspoken criticism of their lot, and more and more of them are lashing back verbally in the open at the Government which has handled the whole problem of medical care so ineffectively.

The relationship of the medical profession in our United States to the economic and organizational aspects of its work now shows clearcut parallels to phases through which our British colleagues have already travelled. On the assumption either that governmental provision of medical care is the most satisfactory, or that it is an excellent method for garnering votes, or for both reasons, our federal executive administration is trying to lead us along a road strikingly similar to that along which our British confreres are now dolefully plodding. We physicians can but take our case to the country as a whole, presenting the facts as we see them. We have to overcome a tremendous public bias in favour of receiving vital services ostensibly at little or no

cost. In addition, the spotlight is thrown as never before on the defects of our current system, and salutary pressures are now being brought to bear upon us to undertake remedial measures. Unless we can meet such justified criticisms as those pertaining to the ineffective coverage provided by most forms of voluntary health insurance, all of these schemes may be deluged by an avalanche of votes in favour of government controlled compulsory measures. Those with grievances against individual doctors or groups of doctors now have little opportunity to be heard usefully short of legal action. Ought not our medical establishment provide the machinery for improving public relations and exposing and rectifying our own errors? We hope to preserve the right of each man to act as an individual in accordance with his own lights to improve the quality of medical care he renders. But unless we are also capable of determined unanimity both in the correction of our faults as well as against encroachment on our individual autonomy, we shall run the risk of losing it.

WILLIAM H. SWEET, M.D.

EDITOR'S NOTE: Dr. Sweet is assistant professor of surgery, Harvard Medical School; lecturer in neurosurgery, Tufts College Medical School; associate visiting neurosurgeon, Massachusetts General Hospital.

Bibliotheca Obstetrica

SÄNGER, MAX (1853-1903): Der Kaiserschmitt bei Uterusfibromen nebst vergleichender Methodix der Sectio Caesarea und der Porro Operation, Leipzig, Engelmann 1882.

Sänger was the first to recognize the importance of a water tight closure of the uterine wound in the Cesarean operation. He studied all the cases of Cesarean section that had been collected by Harris and others. Harris had emphasized the importance of early operation, but had not grasped the importance of sutures. Sutures were almost universally considered to be harmful. Spencer Wells and Robert Barnes each devised technics for removing the uterine sutures on the third day. Sänger, with his careful analysis of the reported cases and with the performance of one successful case, revolutionized the Cesarean operation.

Max Sänger was born in Bayreuth. He graduated in Leipzig in 1875, where he was a pupil of Credé. For most of his life he taught at the University of Leipsig. In 1899 he became Ordinarius and President of the Gynecological Clinic at Prague. He was co-editor of the *Archiv für Gynäkologie.*

For portrait see Thoms' Classical Contributions to Obstetrics and Gynecology.

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NITROGEN MUSTARD TREATMENT OF HODGKIN'S DISEASE*

H. ST. GEORGE TUCKER, JR., M.D.,
and
WILLIAM R. KAY, M.D.,
Richmond, Virginia.

Under the sponsorship and coordination of the Committee on Growth of the National Research Council a widespread clinical study of the nitrogen mustard compounds has been going on for the past four years. A large number of investigators have taken part in this work. Reports from many of these groups have been published[1-9], and from time to time Dr. Cornelius Rhoads, chairman of the Committee on Growth, has summarized the clinical status of these substances[10-11].

From the observations thus far it is clear that the nitrogen mustards have some degree of usefulness in the treatment of lymphomas, leukemias, and allied disorders. Of the various conditions treated, Hodgkin's disease has shown the most promising results. In no sense is nitrogen mustard curative in this condition, but a considerable palliative effect has been obtained in most of the patients treated. More precise evaluation of this palliative effect is needed, and the exact sphere of usefulness of nitrogen mustard in relation to irradiation and other forms of treatment remains to be defined.

In this paper we wish to review briefly the nature and mode of action of nitrogen mustard, and to present observations on twenty-four patients with Hodgkin's disease treated with this substance.

THE NITROGEN MUSTARDS

The term "nitrogen mustard" refers to a class of chemical compounds having as their essential feature the beta-chloroethyl amine group. Two of these compounds, methyl bis (beta-chloroethyl) amine hydrochloride and tris (beta-chloroethyl) amine hydrochloride, have been given extensive clinical trial. These are commonly referred to as HN_2 and HN_3. The former appears to have less toxic effect[5], and is generally preferred. HN_2 was used in our cases. The material is obtained by application to the Committee on Growth of the National Research Council.

From the Department of Medicine, School of Medicine, Medical College of Virginia, and the Medical Service, Veterans Administration Hospital, Richmond, Va.

*Read before the annual meeting of the Medical Society of Virginia, in Richmond, October 18-20, 1948.

The nitrogen mustards are stable in crystalline form, but when put into solution undergo a series of rapid polymerizations. The intermediate products of these reactions have the desired potent cytotoxic effect, while the end products are relatively inert. For this reason it is necessary that the material be administered to the patient promptly after being put into solution.

The biological effects of the nitrogen mustards are strikingly similar to those of irradiation. Both have a cytotoxic effect predominantly on rapidly proliferating cells. Both appear to affect primarily the cell nucleus, and specifically to inhibit cell mitosis. It is thought that the action of the nitrogen mustard compounds is due to inhibition of some enzyme system of the chromosomes.

Nitrogen mustard produces damage chiefly to lymphoid and hematopoietic tissue. This is the basis of its therapeutic effect, but the accompanying bone marrow damage limits the amount that can be safely given. Unfortunately, the margin between effective and toxic dosage is narrow.

DOSAGE AND ADMINISTRATION

The usual course of treatment with nitrogen mustard consists of four intravenous injections of 0.1 mg. per kg. of body weight, given on successive days. Some investigators have given as many as six injections, but this amount increases the risk of severe bone marrow depletion. Studies are in progress on the effects of larger single doses in treating highly malignant neoplasms. In our cases, the dosage of four injections of 0.1 mg. per kg. each was used. With a few of the earlier patients injections were given every other day, but most of the patients were treated daily.

The best method of administration seems to us to be the injection of the mustard solution into the tubing of a running saline intravenous infusion, as recommended by Goodman et al[2]. The saline infusion is begun, then the nitrogen mustard solution is prepared and within five minutes the required amount is injected into the tubing. This technique allows prompt administration with adequate dilu-

tion, and minimizes the possibility of extravasation of the highly toxic agent.

TOXIC REACTIONS

The toxic reactions to nitrogen mustard are listed in Table I.

TABLE I: TOXIC EFFECTS OF HN_2

1. Thrombosis of vein
2. Nausea and vomiting
3. Blood depression
   a. Initial lymphopenia
   b. Late neutropenia and thrombopenia
   c. Anemia
   d. ? coagulation defect

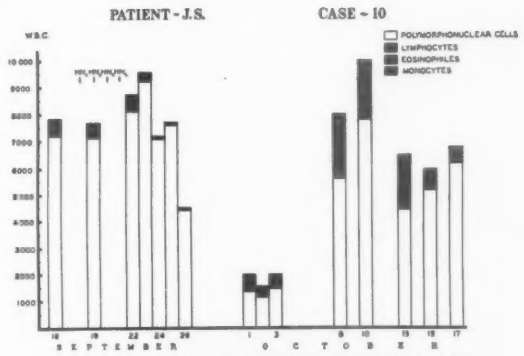
We believe that thrombophlebitis of the injected vein can be almost entirely eliminated by the use of the above technique of administration. It was encountered twice when the nitrogen mustard solution was injected directly into the vein, but in no case after the above method was adopted.

Nausea and vomiting occurred regularly in every one of our patients, beginning soon after the injection and lasting for several hours. Diarrhea was less common. These symptoms are apparently due to a direct toxic effect of nitrogen mustard on the gastro-intestinal mucosa[5]. They were usually not severe, and almost always subsided by the following day. In a few instances, the subsequent injection was deferred for one day because the patient remained weak, but in no case was it necessary to stop treatment. The use of atropine and sodium phenobarbital seemed to allay the gastro-intestinal reaction.

By far the most serious toxic effect of nitrogen mustard is the damage to blood forming tissue. This is the limiting factor which prevents the use of larger and perhaps more effective doses. All the elements of the peripheral blood may show this effect.

The leukocytes usually show an initial lymphopenia beginning soon after treatment and lasting only a few days. During the third week after treatment neutropenia develops with a drop in the total leukocyte count. This is of variable severity. The leukopenia usually lasts about a week, after which the blood returns to normal (Fig. 1).

These changes were observed in all our patients, although in some they were very slight. The total leukocyte count fell usually to around 3,000 or 4,000. In five cases, the leukocyte count fell to



SERIAL WHITE BLOOD CELL AND DIFFERENTIAL COUNTS FOLLOWING NITROGEN MUSTARD THERAPY

Fig. 1

below 2,000, the lowest being 1,300 with 40% neutrophiles. None of these patients showed any symptoms of neutropenia, but transfusions were given to a few. In all cases the blood count returned to its former level in about one month. When leukopenia was present before treatment, the leukocyte depression was no more severe than when the initial count was normal, and the blood count subsequently returned to about the pre-treatment level.

Some degree of depression of the platelet count was observed in two-thirds of our patients. This occurred during the second and third weeks and roughly paralleled the neutropenia. In five patients the platelet count fell to below 50,000, and in four of these petechiae were noted. These promptly disappeared after transfusions.

Anemia has been described as a toxic effect of nitrogen mustard, but most of our patients showed very little change in red cell counts after treatment. One patient did develop a severe anemia which may have been caused by the drug or may have been due to his disease. When severe anemia was present before treatment, transfusions were given before nitrogen mustard was begun.

Recently the occurrence of a blood coagulation defect following nitrogen mustard therapy has been reported[12]. No studies of clotting time were made in our patients. However, no hemorrhagic phenomena were observed other than the petechiae mentioned above.

CLINICAL RESULTS

Twenty-four patients with Hodgkin's disease were treated during the period from April, 1946, to July, 1948. Of these, five were treated at the Medi-

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TABLE II: SUMMARY OF DATA ON PATIENTS TREATED

Case	Patient	Age	Race and Sex	Duration of Disease	Previous Irradiation	Extent of Involvement	Most Prominent Symptoms	Results of HN2 Treatment: Course #1	#2	#3	Duration of Remissions: #1	#2	#3	Final Status: Time After First Course of HN2	
1	B.E.	14	C.F.	3 yrs.	0	Cervical, abdominal	Fever, wt. loss	Good	Good	Fair	4 mos.	4 mos.	1 mo.+	Living	2½ yrs.
2	W.McG.	35	W.M.	6 mos.	0	Generalized	Fever, wt. loss	Good	Fair		2 mos.	1 mo.		Died	6 mos.
3	O.J.	43	C.M.	1 yr.	0	Generalized	Fever, wt. loss, pain	Good	Fair		3 mos.	?		Living	4 mos.
4	H.R.	23	W.M.	5 yrs.	+	Mediastinal, abdominal	Fever, wt. loss, hemoptysis	Fair	Fair		1 mo.	½ mo.		Died	3½ mos.
5	E.S.	52	C.M.	2 yrs.	0	Generalized, incl. lung	Fever, wt. loss	None			0			Died	2 mos.
6	W.C.	49	W.M.	3 mos.	0	Abdominal, mediastinal	Fever, wt. loss	None			0			Died	2½ mos.
7	I.E.	6	C.M.	6 mos.	0	Generalized	Fever, wt. loss, jaundice	None			0			Died	2 days
8	C.P.	51	W.M.	10 yrs.	+	Generalized, incl. bone	Fever, wt. loss, pain	Good	Good	Fair	6 mos.	3 mos.	1 mo.	Living	15 mos.
9	H.G.	25	C.M.	2½ yrs.	+	Cervical, abdominal	Fever, wt. loss	None			0			Died	18 days
10	J.S.	30	W.M.	3 yrs.	+	Generalized, incl. lung	Fever, wt. loss	Fair	Fair		2 mos.	1 mo.		Died	5 mos.
11	C.W.	25	W.M.	2½ yrs.	+	Generalized	Fever, wt. loss, jaundice	None			0			Died	3 weeks
12	G.S.	43	W.M.	1 yr.	0	Generalized	Fever, wt. loss, vomiting	Good	None		1½ mos.	0		Died	4 mos.
13	S.S.	37	W.M.	4 mos.	+	Generalized, incl. lung	Fever, wt. loss, pain	Good	Fair	None	2 mos.	1 mo.	0	Died	6 mos.
14	E.C.	24	W.M.	6 mos.	+	Cervical, abdominal	Wt. loss, dysphagia	None			0			Died	10 days
15	H.M.	40	W.F.	2 yrs.	+	Generalized, incl. lung	Fever, wt. loss, pain	Good	Good		4 mos.	1 mo.		Died	11 mos.
16	A.L.	50	W.M.	4 yrs.	+	Mediastinal, cardiac	Fever, wt. loss, dyspnea	Fair	None	None	1½ mos.	0	0	Died	5 mos.
17	C.M.	45	W.F.	3 yrs.	+	Generalized	Wt. loss, pain, edema	Fair	Good	Good	1 mo.	1 mo.	1 mo.	Living	10 mos.
18	F.B.	47	W.M.	1 mo.	+	Generalized, incl. skin	Wt. loss, pain, cough	None			0			Died	1 mo.
19	A.R.	68	W.M.	6 yrs.	+	Intestinal	Fever, pain, vomiting	Fair			½ mo.			Died	1 mo.
20	M.K.	23	W.F.	5 yrs.	+	Abdominal	Fever, wt. loss	Good			?			?	
21	E.H.	64	W.F.	6 mos.	+	Generalized	Fever, wt. loss, pain	Good	Fair		1 mo.	1 mo.		Living	3 mos.
22	M.B.	58	W.M.	1 yr.	+	Generalized	Fever, wt. loss, pain	Fair	None		½ mo.	0		Died	3 mos.
23	J.B.	19	W.M.	1½ yrs.	+	Generalized	Fever, wt. loss, pain, edema	None			0			?	
24	H.C.	35	W.M.	3 yrs.	+	Generalized, incl. bone	Wt. loss, pain	Good	Good		9 mos.	2 mos.		Living	13 mos.

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cal College of Virginia Hospital, eleven at the Veterans Administration Hospital, Richmond, Virginia, and eight by physicians in other hospitals who have kindly supplied us with detailed reports.

Table II summarizes the clinical data on these patients. The diagnosis of Hodgkin's disease was established in all cases by biopsy. In twenty cases the biopsy report was Hodgkin's granuloma, and in four (cases 6, 7, 14, and 22) Hodgkin's sarcoma. In one patient (case 5) progression from the granulomatous to the sarcomatous stage was observed.

In all cases the disease had become widely disseminated, and in all cases definite symptoms were present. There was considerable variation, however, in the apparent rate of progression. In some (e.g., cases 1, 8, and 24) the disease appeared to be very slowly progressive, and the general condition of the patient was good. In others (e.g., cases 2, 6, 14, 18) the duration of the illness had been brief and the course rapidly downhill.

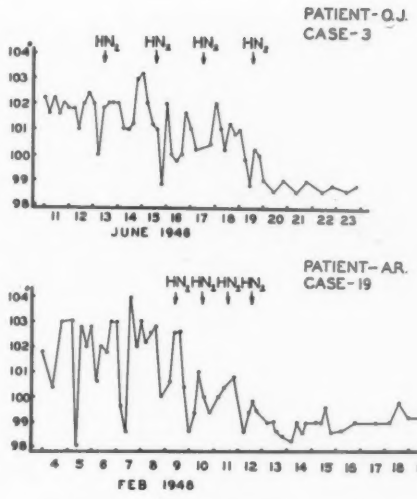
Seventeen patients had received previous irradiation. In these irradiation had become ineffective, either because of true radio-resistance of the tumor or because of wide dissemination. The other seven had had no previous therapy. Nitrogen mustard was given because the widespread involvement made irradiation seem impractical.

There can be no doubt that nitrogen mustard has a very definite effect in Hodgkin's disease. Some patients showed no change at all after treatment, but in most some type of beneficial effect was seen.

Symptomatic improvement was most striking. All the patients who showed any response felt definitely better after treatment. Their appetites improved and they felt stronger. Progressive weight loss was checked and in several instances a marked gain in weight followed treatment.

Fever was relieved in twelve out of twenty patients who were febrile. In some cases the temperature became normal after the first injection. More commonly, fever subsided by lysis over a five or six day period (Fig 2). Cessation of fever brought relief of sweats, headache, and malaise.

Pain was not a common symptom but was present in ten patients. These had pain referable to superficial nodes, or to pleural, abdominal, or vertebral lesions. In eight of these patients pain completely subsided after nitrogen mustard treatment. One patient who was bedridden with painful vertebral lesions was completely relieved and walked normally after treatment although x-rays showed further extension of vertebral destruction (case 24).



RESPONSE OF FEVER IN HODGKIN'S DISEASE TO NITROGEN MUSTARD

Fig. 2

Objective improvement was definite but less striking than the symptomatic relief. Enlarged lymph nodes generally showed softening and regression in size (Fig 3). Resolution of the nodes was not always complete. Enlarged livers and spleens became smaller but in most instances did not subside entirely to normal. Enlarged mediastinal nodes showed some decrease in size but did not entirely disappear. In general, large tumor masses did not respond very well to nitrogen mustard.

Fig. 3. Nitrogen mustard 5.1 mg. given daily for 4 days 5-21-48 to 5-24-48. Note marked decrease in size of mass of cervical nodes.

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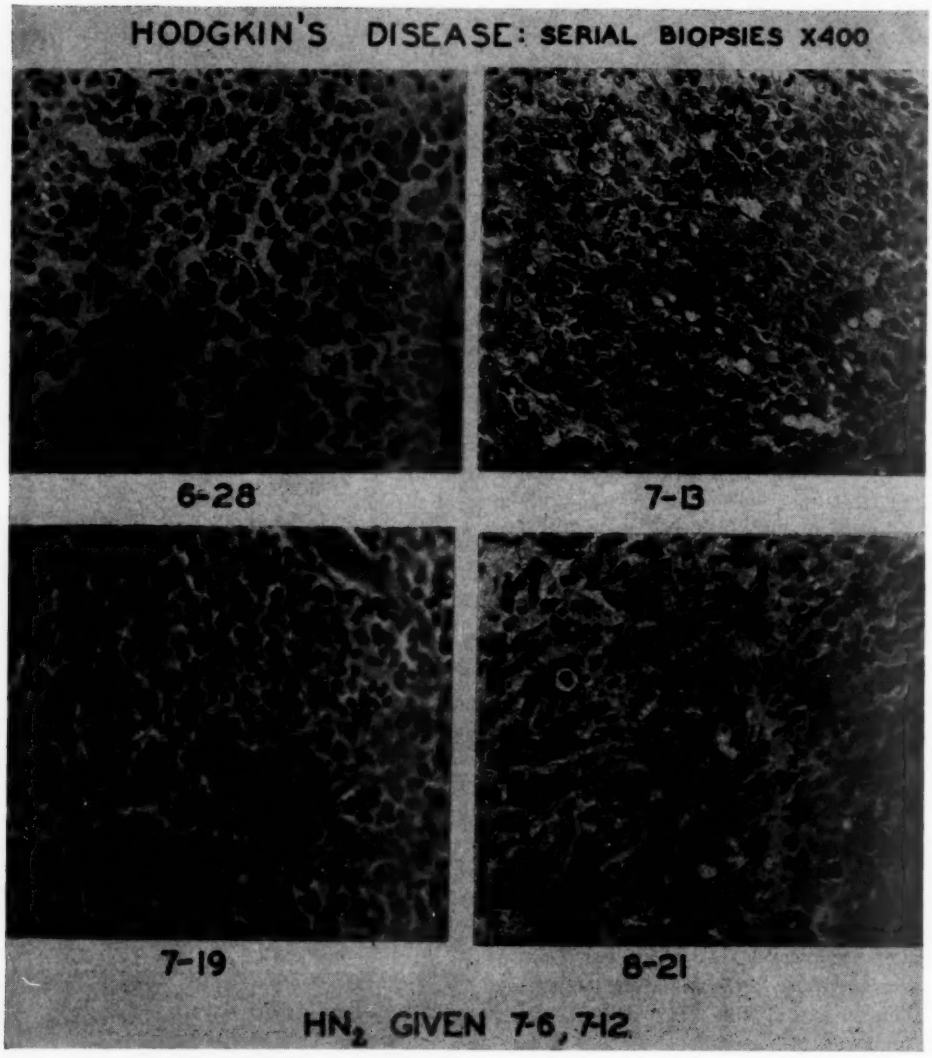

Fig. 4. Serial biopsies illustrate degenerative changes in Hodgkin's tissue in lymph nodes following nitrogen mustard with subsequent recovery of tumor. (See text)

Four patients with pulmonary infiltrations were treated. One of these (case 15) showed striking improvement. Two (cases 10 and 13) showed no response but were later found at autopsy to have a complicating tuberculosis. The fourth patient (case 5) was unimproved, and subsequently was found to have progressed to the sarcomatous stage of the disease. One patient with pericardial effusion (case 16) showed dramatic subsidence of fluid and relief of tamponade after treatment.

One patient with Hodgkin's disease of the skin (case 18) showed no improvement after nitrogen mustard, while skin areas which were irradiated cleared considerably.

Serial lymph node biopsies were obtained before and after treatment in case 5 (Fig. 4). The initial biopsy showed a typical Hodgkin's granuloma. This patient showed a very poor clinical response to treatment, but nevertheless marked degenerative changes are seen in the node removed immediately after completion of therapy. In the third biopsy a week later, the tumor tissue appears to be recovering. A

fourth biopsy one month later shows a definitely sarcomatous lesion. The transition from granuloma to sarcoma is fairly often seen in Hodgkin's disease, and there is no particular reason for believing that nitrogen mustard was responsible for this change.

In general, the effect of nitrogen mustard in Hodgkin's disease is the production of some type of remission. The remissions that we observed varied considerably in completeness and in duration. Inevitably, symptoms and evidence of progression of the disease recurred. When the initial response justified it, recurrences were again treated with nitrogen mustard. Treatment was not repeated within a month because of the danger of cumulative depression of the bone marrow. We know of no limit to the number of courses of treatment that may be given if the patient continues to respond and does not develop bone marrow depletion. However, to date none of our patients has had more than three courses.

In Table II, we have attempted to evaluate the total beneficial effect to the patient of each course of treatment. Results are listed as good where the patient very definitely improved both subjectively and objectively. Most of these patients became free of symptoms and were able to leave the hospital and resume some sort of activity. Results are listed as fair where definite improvement was seen but the remission was incomplete or very brief. Results are listed as none where the effects were either absent or so slight as to be of no benefit to the patient.

TABLE III: SUMMARY OF RESULTS

	Course #1	Course #2	Course #3
Good	10	5	1
Fair	6	6	2
None	8	3	2
	24	14	5

These results are summarized in Table III. On the initial course of treatment, results were considered good in ten patients, fair in six, and none in eight. These figures mean very little statistically, but give some idea of the results to be expected in treating this type of patient. It will also be seen that results were poorer with successive courses of treatment.

The durations of the remissions produced are listed in Table II. These have been disappointingly brief. While some longer remissions occurred, the mean duration is about six weeks. With successive courses of treatment, remissions tend to become briefer until finally no response is obtained.

Most of the patients treated have subsequently died. It does not appear to us that nitrogen mustard treatment has appreciably prolonged their lives. It has undoubtedly restored many of them to at least temporary comfort and hope.

DISCUSSION

These results are not at first impressive. But considering the type of patients who were treated, we believe that nitrogen mustard has been definitely useful. Most of these patients could have received palliation by no other means. Some of them might have been equally well treated with irradiation.

It seems to us that the results obtained are most closely correlated to the rate of progression of the disease. In the slowly progressive case, nitrogen mustard produces a good response and the remission may be of considerable duration. In the more malignant or rapidly progressive case, the response is poorer and the remission briefer. In the sarcomatous form of Hodgkin's the results are very poor. The underlying course of the disease is not altered. This is probably equally true of irradiation or of any other palliative measure that does not eradicate the disease.

The effect of nitrogen mustard on individual lymph nodes appears to us to be less than could be expected from irradiation. For this reason irradiation remains the treatment of choice in localized disease, or where, although spread has taken place, all the nodes are still accessible to irradiation. In very early localized disease radical surgery followed by irradiation should be considered.

Where large tumor masses are present, and may be causing pressure symptoms, we believe that irradiation will be more effective than nitrogen mustard.

When the disease has become widely disseminated and particularly where abdominal involvement is present, results with irradiation are usually poor. These are the cases where nitrogen mustard is most useful. The presence of severe symptoms, particularly fever, is usually indicative of involvement of internal nodes. In these cases, nitrogen mustard may give very gratifying results.

Figure 5 illustrates our conception of the difference in the effects of irradiation and nitrogen mustard.

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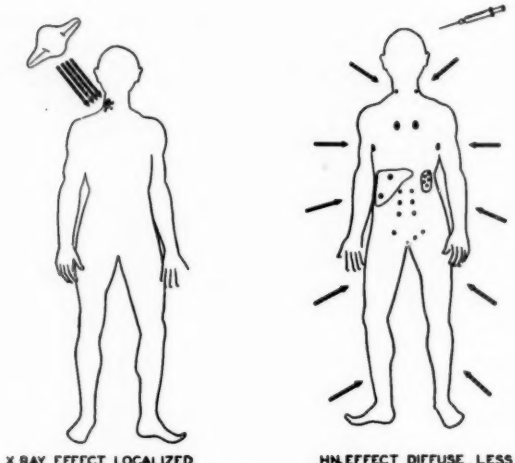

Fig. 5. Our impression of the difference in effects of irradiation and nitrogen mustard.

Irradiation exerts a more concentrated effect, in more readily controlled dosage, and is preferred in localized disease. Nitrogen mustard has perhaps a less concentrated effect in present dosages, but acts throughout the body and is preferred where widespread disease is present.

It is apparent that the present dosage of nitrogen mustard is ineffective against highly malignant forms of Hodgkin's disease. This applies also to other highly malignant lymphomas such as lymphosarcoma and reticulum cell sarcoma. In seeking palliation for these patients, we must accept greater risks. Studies are in progress of the effects of larger single injections of nitrogen mustard combined with irradiation in these cases.

CONCLUSIONS

1. The nature and mode of action of the nitrogen mustard compounds are reviewed.
2. Observations are presented on the treatment with nitrogen mustard (HN_2) of twenty-four patients with disseminated Hodgkin's disease.
3. Nitrogen mustard had a definite palliative effect in two-thirds of these patients.
4. Irradiation is the treatment of choice in localized or still accessible Hodgkin's disease.
5. Nitrogen mustard is the treatment of choice where widespread dissemination of the disease has occurred.
6. Nitrogen mustard in the present dosage is ineffective against highly malignant or sarcomatous Hodgkin's disease.

BIBLIOGRAPHY

1. Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the Beta-Chloroethyl Amines and Sulfides. *Science* **103**:409, 1946.
2. Goodman, L. S., Wintrobe, M. M., Dameshek, W., Goodman, M. J., Gilman, A., and McLennon, M. T.: Nitrogen Mustard Therapy; Use of Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride and Tris (Beta-Chloroethyl) Amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, and Allied and Miscellaneous Disorders. *J.A.M.A.* **132**:126, 1946.
3. Jacobson, L. O., Spurr, C. L., Barron, E. S. G., Smith, T., Lushbaugh, C., and Dick, G. F.: Nitrogen Mustard Therapy; Studies on the Effect of Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride on Neoplastic Diseases and Allied Disorders of the Hemopoietic System. *J.A.M.A.* **132**:263, 1946.
4. Alpert, L. K., and Peterson, S. S.: The Use of Nitrogen Mustard in the Treatment of Lymphomata. *Bull. U. S. Army Med. Dept.* **7**:187, 1947.
5. Karnofsky, D. A., Craver, L. F., Rhoads, C. R., and Abek, J. C.: Evaluation of Methyl-Bis (Beta-Chloroethyl) Amine Hydrochloride and Tris (Beta-Chloroethyl) Amine Hydrochloride (Nitrogen Mustards) in the Treatment of Lymphomas, Leukemia, and Allied Diseases. Approaches to Tumor Chemotherapy. *Am. Assoc. for the Advancement of Science,* pp. 319-337, 1947.
6. Wintrobe, M. W., Huguley, C. M., Jr., McLennon, M. T., and Lima, L. P. de C.: Nitrogen Mustard as a Therapeutic Agent for Hodgkin's Disease, Lymphosarcoma, and Leukemia. *Ann. Int. Med.* **27**:529, 1947.
7. Wilkinson, J. F., and Fletcher, F.: Effect of Beta-Chloroethylamine Hydrochloride in Leukemia, Hodgkin's Disease, and Polycythemia Vera. *Lancet* **2**:540, 1947.
8. Craver, L. F.: Recent Advances in Treatment of Lymphomas, Leukemias, and Allied Disorders. *Bull. N. Y. Acad. Med.* **24**:3, 1948.
9. Sherry, M.: Nitrogen Mustards in the Treatment of Hodgkin's Disease and Lymphosarcoma. *Sou. Med. Jour.* **41**:118, 1948.
10. Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Disease. *J.A.M.A.* **131**:656, 1946.
11. Rhoads, C. P.: Report on a Cooperative Study of Nitrogen Mustard (HN_2) Therapy of Neoplastic Disease. *Trans. Assoc. Am. Ph.,* **60**:110, 1947.
12. Smith, T. R., Jacobson, L. O., Spurr, C. L., and Allen, J. G.: A Coagulation Defect Produced by Nitrogen Mustard. *Science* **107**:474, 1948.

DISCUSSION

DR. BYRD S. LEAVELL, Charlottesville: Dr. Tucker has given an excellent discussion of the use of nitrogen mustard in the treatment of Hodgkin's disease. The experience which Drs. Kay and Tucker report in 24 patients with Hodgkin's disease is very similar to that which we

have had at the University of Virginia Hospital. The authors are very conservative in drawing conclusions. Perhaps it is worth emphasizing that the patients which have received this form of treatment have been patients in the terminal stages of disease or patients with widespread disease. Usually they had become refractory to other forms of treatment. The prognosis in this type of individual is quite different from the individual with localized untreated disease. The fact that no prolongation of life has been demonstrated is no serious criticism of this form of therapy since irradiation and other forms of therapy, even in the milder forms of disease, probably do not prolong life more than a few months. The fact that nitrogen mustard does have some effect on these individuals is the important thing. The dramatic clinical improvement that occurs in some of these patients, the cessation of pain, the disappearance of fever, the improvement in well being, are more impressive in the various individuals than the statistical results. Even more important is the hope that some compound with action similar to that of nitrogen mustard will be developed and will have less toxic reaction and a better therapeutic effect.

We have seen no toxic reactions except those associated with nausea and vomiting and leukopenia. As a rule the nausea and vomiting occurred one and a half to two hours after the injection and it has been possible to treat some patients on out-patient basis with this drug. If they have time to rest for half an hour and then reach home before the nausea and vomiting begins, we find no objection to treating these individuals when they are not confined to the hospital.

The course of disease in some of our patients has suggested that sensitivity to x-ray therapy was regained. Other authors have reported similar observations. The effect of combined x-ray and nitrogen mustard therapy has not been evaluated. I would like to ask Dr. Tucker if he has observed any incident of aggravation of symptoms following nitrogen mustard therapy. We had become accustomed to looking out for swelling in mediastinal tumors treated with x-ray, but felt that such a reaction was very unlikely with nitrogen mustard. We have recently seen an individual with Hodgkin's disease who had an extradural tumor in the spinal canal who developed complete block and progression of symptoms on two occasions after a course of nitrogen mustard therapy.

DR. J. POWELL WILLIAMS, Richmond: I should like to discuss very briefly the group of cases Dr. Tucker mentioned in his paper who received larger doses of mustard in combination with x-ray. I brought some films with me, but I do not see an illuminator, so will not be able to show them.

The first case was a patient who came up from North Carolina who had had a biopsy with marked increase in rate of growth immediately afterward. The histopathological diagnosis was lymphosarcoma. At that time, the mass was about the size of an orange, located in his right groin, and fungating through the biopsy wound. He was given 0.3 mg. of nitrogen mustard per kg. body weight, which is three times the usual dose. Within thirty minutes, he was gotten to the x-ray room and was given 1,000 r units of x-ray. The mass melted away like magic. It might have done so with nitrogen mustard alone or with x-ray alone, but nevertheless the recession was spectacular.

The next case was a man with a mass in the neck. It was not a large mass and could not account for the very high Pel-Ebstein type of temperature which went to 104 and 105 degrees. We concluded that he had a mass of glands in his retroperitoneal space, although we could not demonstrate them. So he was treated with nitrogen mustard and x-ray to the abdomen, the same dosage as above being used. On the fourth day his temperature returned to normal and his recovery was uneventful. Biopsy in this case showed Hodgkin's disease.

In the third case, I do not know exactly what the diagnosis is because the pathologists let us down. He was diagnosed as lymphoblastoma at Duke. We disagree with that diagnosis and preferred neuroblastoma. He has had four biopsies since which have only added to the confusion. He was treated with x-ray and the first time got a very good result and was sent home on a thirty-day leave. He came back after twenty-eight days because the mass in his left axilla had begun to grow again. He was treated again and sent home but returned in less time. Each time thereafter the period of remission was shorter. On the most recent admission, he presented a mass near the mid-line of the neck which displaced both the trachea and esophagus and made swallowing difficult, so we decided to augment our efforts by the use of nitrogen mustard. He was given 0.3 mg. per kg. intravenously and then taken immediately to radiology. Just as he was rolled in, the machine broke down. The roentgenologist, being a smart doctor, put him on the table anyway because he had been there before and knew what to expect. He got no radiation whatever, but the response to the mustard alone was good. The mass in his neck subsided and he experienced great relief, but today—thirteen days after treatment—he is complaining again of dysphagia.

The fourth case was a man of 23 with inoperable carcinoma of the lung whose tumor had continued to grow rapidly in spite of enzyme block and intensive x-ray therapy. He was finally given 0.3 mg. of nitrogen mustard per kg. intravenously and within half an hour 1000 r units of roentgen therapy through two portals. The disease did not falter in its stride and he continued rapidly downhill to his death.

The fifth case, a negro of 48 with adenocarcinoma of the rectosigmoid with metastases to the liver and lungs, was treated with the hope that the nitrogen mustard might render these notoriously resistant tumor cells more vulnerable to x-ray. He received two intravenous injections of nitrogen mustard combined with x-ray therapy with an interval of three weeks between. Both the liver mass and the x-ray shadows of the lung metastases increased in

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size during treatment and he went on to death just as rapidly as if he had received no treatment at all; if not more so.

This was the only case so far treated in which the white blood count dropped below 1000 per cmm. It hit a low point of 750 per cmm. on the tenth day after the first treatment, but returned rapidly to a normal of 8000 before the second treatment. It was 10,000 at the time of death, with 180,000 platelets and 12 grams of hemoglobin.

The sixth and last case to be reported was a young white man who had had a mass in the lower third of the femur for more than two years which from x-ray examination had been thought to be benign cystic disease. It was finally biopsied and still there was doubt as to its true nature; a second biopsy was reported by the Army Institute of Pathology to be fibrosarcoma and the leg was amputated, but this time there were metastases in the lung and he was transferred to us for roentgen therapy. Because of the resistant nature of such tumors to the x-ray, it was more or less expected that little would be accomplished by this means alone, but it was started and continued until it was obvious that the original metastases were growing and new areas appearing. Then enzyme block was added with the same lack of results. Finally, nitrogen mustard 0.3 gm. per kilo followed by roentgen therapy 1200 r units through three portals within half an hour was super-added, but the disease progressed unabated to death.

Our limited experience would seem to indicate that nitrogen mustard even in relatively large doses is ineffective save in tumors of lymphoid origin and we have been unable to show as yet that the combined therapy offers any significant advantage over older methods. We have at present a group of eight or ten patients still under observation and expect to continue clinical investigation along these lines in the hope the future and more extensive experience may offer more encouragement.

NOTE:

12/30/48.—The first three patients in whom initial good results were reported have all since died of their disease. Patient No. 3, in whom the diagnosis was in doubt, has come to autopsy and apparently had an anaplastic carcinoma arising from the left main bronchus.

DR. WM R. KAY: In an article entitled "A Coagulation Defect Produced by Nitrogen Mustard", published in *Science* (**107**:474, 1948, May 7), the authors (T. R. Smith, L. O. Jacobson, C. L. Spurr, J. G. Allen, and M. H. Block) point out that in certain patients (and normal rabbits) nitrogen mustard therapy may produce a prolongation of whole blood coagulation time similar to the effect of ionizing radiation. The defect is due to the appearance of an anticoagulant in the blood biologically indistinguishable from heparin. Five patients with neoplastic disease treated with nitrogen mustard developed a prolongation of the coagulation time and two of the patients died, having diffuse large hemorrhages. Two of these patients received 0.1 mgm./kg. daily for four days, one received four injections of 0.1 mgm./kg. every 12 hours, one received four injections of 0.1 mgm./kg. at seven-hour intervals, and one received two injections of 0.3 mgm./kg. at six-hour intervals. It was not stated which patients died, but in view of the fact that, as Dr. Williams mentioned, larger doses are now being used in some patients, it might be worthwhile to determine coagulation times in these patients. The coagulation defect can be controlled by the intravenous administration of toluidine blue or protamine.

As regards the beneficial effects of nitrogen mustard in Hodgkin's disease, Rhoads, in his most recent summary, states that subjective improvement is seen in about 90 per cent of the patients treated, and objective improvement in about 75 per cent.

As Dr. Tucker points out, thromboses at the site of administration of the drug may be avoided by use of the method outlined.

I would like also to emphasize that the drug should be freshly prepared for each administration and any excess should be discarded.

DR. TUCKER, closing the discussion: We have not noticed preliminary swelling of tumor masses treated with nitrogen mustard, such as sometimes occurs following irradiation. We have thought that nitrogen mustard might be preferable to irradiation in the patient with a large mediastinal mass with tracheal compression, where even transient swelling and edema might endanger life. Further study of the early changes in lymph nodes following nitrogen mustard will be necessary to decide this point.

We did have one patient with Hodgkin's involving the pleura who developed a large bloody pleural effusion following nitrogen mustard treatment. It is possible that degeneration of the tumor tissue might lead to such undesirable results.

Dr. Williams has mentioned the use of large single doses. We are employing the single dose method now, giving usually 0.3 mg. per kilogram of body weight. We have treated only a few patients in this way. In some the results seem better than with the repeated smaller doses. In patients with large tumor masses we are using a single large dose of mustard combined with a single heavy dose of irradiation.

I agree with Dr. Kay that we should follow the clotting time especially when using the larger doses of mustard.

PROTEIN DEFICIENCY IN SURGICAL PRACTICE*

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Since the beginning of human history the loss of blood has been regarded invariably as a serious threat to life, but only within our memory has the loss of the non-cellular or liquid constituent of the blood received consideration. In the not too distant past, blood has been regarded as a physiological fluid consisting of cells suspended in plasma functioning as a unit and the possibility that the fluid could be lost without the cells received scant notice until Epstein conclusively showed that loss of proteins was associated with edema; Whipple[1] and his associates, by animal experimentation, stressed the vital part that plasma played in many body functions and explained many physiological and pathological manifestations which had previously baffled the profession.

Another deterrent to our progress has been the lack of a medium with which we could compensate for the loss of protein. As noted above, Whipple was one of the pioneers who focused our attention upon the value of proteins in maintaining nutrition, but he went further and pointed out that protein was essential in repelling and curing infections. Ravdin[2] investigated some surgical aspects of protein, and his contributions will be referred to again.

In various surgical conditions the average requirement of protein may be altered to a variable degree, but it can be stated as a principle that any unusual demand upon the body protein will be reflected in the level or content of the protein in the plasma; therefore, the protein level may be regarded as an index of the reserve, which may be depleted until it reaches a critical level. Brief illnesses and minor operations do not as a rule upset the reserve, and any temporary deficiency is met by the normal physiological response plus alimentation. For example, an interval appendectomy or a simple herniorrhaphy will show a negative nitrogen balance for a few days, during which time the patient receives little food and may vomit occasionally. He depends upon the stored-up proteins to meet the temporary increased demand. We[3] have reviewed a series of such cases and have shown that the amount of nitrogen excreted is in excess of the nitrogen intake, parenterally or otherwise, and usually the patient is in a negative balance or sustains a net loss of nitrogen. Just as soon as the patient can assimilate adequate food, his nitrogen balance is adjusted; and, should he gain weight, there may exist a positive nitrogen balance.

There are three sources of proteins within the body which can be drawn upon by the normal physiological mechanism, both in health and disease. Whipple[5] classifies them as: (1) Labile reserve, which is quickly and readily appropriated, (2) Dispensable reserve, largely residing in the muscles, (3) Indispensable or fixed tissue protein, a constituent of the liver. The mechanism by which these classes of proteins become available is complex and often modified, and even nullified by organic disease. Proteins can be regenerated even in low constitutional states and in the absence of adequate protein intake. In the presence of a long continued drain on the protein mechanism, the level reaches a low point and is often arrested, suggesting some sort of protective mechanism.

The average healthy individual maintains his protein level by an adequate diet and can meet the emergency of minor and brief major operations without serious depression of his nitrogen balance or plasma protein. We are more concerned with the patient whose proteins are depleted and must submit to operative measures. That such situations are not uncommon is borne out by our observations of consecutive cases admitted to Gallinger Hospital, which showed that, in 50 cases on admission, the protein level was subnormal in 16.5% of cholecystitis; 33 per cent in carcinoma of the stomach, and 33 per cent in cases on non-bleeding duodenal ulcers. Other clinicians had similar experiences.

These are some of the factors which are concerned in the reduction of plasma protein:

(1) Inadequate intake, which may arise from a variety of circumstances, such as voluntary restriction, starvation, anorexia, chronic alimentary obstruction.

*Read before the annual meeting of the Medical Society of Virginia in Richmond, October 18-20, 1948.

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(2) Mal assimilation such as may arise from diseases of the stomach and pancreas.

(3) Failure of the protein forming mechanism, seen most frequently in diseases of the liver.

(4) Excessive loss by the way of a gastro-intestinal fistula, diarrhea, excessive emeses, gastro-intestinal tubal aspiration, constitutional diseases, malignancies.

(5) Immoderate demands by hypermetabolism, noted in thyroid disease, protracted fevers and excessive physical activity.

Although a few additional causes of protein deficiency could be added, it is not necessary to elaborate on the various items listed, as they are almost self-evident. These would apply to the chronic rather than the acute type of hypoproteinemia, as the deficiency is usually designated. Experience has indicated that 6.5 grams of protein in 100 grams of plasma is a normal percentage for all practical purposes, while the lowest level consistent with a good prognosis is 5.0%—by common consent called the critical level. Between these two levels a state of hypoproteinemia exists, the degree accentuated as it approaches the critical. A single estimation without consideration of dehydration, hemoconcentration, edema, or hemorrhage can be misleading; and all factors contributing to its variation should be evaluated before measures are undertaken to remedy any apparent deficiency. The ratio of the albumin to the globulin in the plasma is roundly two to one, but for practical purposes the ratio can be forgotten in the majority of surgical cases and only the total protein content be estimated. After all, it is the albumin which is the more active fraction and the one that is responsible for most of the problems concerned in meeting protein deficiencies.

Miranda[7] has suggested a classification of nutritional deficiences which has much to recommend it. Those conditions due to insufficient nourishment may properly be divided as follows: (1) Undernutrition, or inadequate caloric intake; (2) Malnutrition or vitamin deficiency; (3) hypoproteinosis, deficiency of protein intake. Miranda proposed the latter name, hypoproteinosis, for which we have been calling hypoproteinemia, and makes a sharp distinction between the two. Hypoproteinemia is a symptom, but not necessarily a constant one, of hypoproteinosis, which in his definition includes many other conditions than low plasma protein levels. Hypoproteinosis includes all those conditions which involve low protein intake; he believes that it affects young children and may be characterized by delay in growth, diarrhea and lack of immunity to disease. Dehydration is often present with its attending low blood pressure, cold extremities and dry skin. His observations and deductions are interesting, if not convincing.

For the clinical consideration of the protein deficit, it is both convenient and practical to consider the acute and chronic states separately, although two may merge. The best example of acute deficiency is hemorrhage, but it should be recalled that serious and sustained loss of plasma alone may be noted in general edema, intestinal obstruction, burns, shock, and dehydration. While these conditions are often met in an acute form, they may assume a chronicity, as in slowly healing burns. Under such conditions complete hemograms, specific gravity of the blood, and hematacrit estimation should be laboratory procedures in addition to determining the protein level.

Plasma volume determination, according to the method of Evans, is without doubt a much more accurate way of assessing the protein content of the blood. Most hospital laboratories are not equipped or not conversant with it, and, consequently, it is not a service the medical or surgical clinician can obtain. It may be established as a routine laboratory procedure in the near future.

The deficiency in the acute conditions is best met by a knowledge of the underlying cause. There is no substitute for blood when blood has been lost, but the use of plasma as a stop gap, when the proper type of blood is unavailable at once, has a definite place in the treatment. When loss of blood is not the exciting cause of hypoproteinemia, then blood must be used cautiously, as its over-use may be attended with packing the capillaries with cells, and the danger of reaction is not negligible. If time is an important factor, we may expect prompt response with a minimal risk. When an emergency does not exist, there are several amino-acid solutions for intravenous use which are reliable; and they can be supplemented by highly concentrated amino-acid mixtures for oral use. The response to this therapy is often satisfactory unless the underlying cause is irremediable. Shock is so frequently associated with hemorrhage that some confusion arises in the differentiation, and in such instances the liberal use of plasma is good therapy, with or without blood; too

much dependence should not be placed upon solutions of electrolytes and glucose, as their effects, insofar as restoring blood pressure are concerned, is fleeting.

The consideration of chronic protein deficiency presents a formidable list of surgical diseases and complications, but it is a phase of surgical preoperative and post-operative treatment that has received sporadic notice. A partial list of the conditions in which we find protein depletion would include post-operative edema, prolonged infections, persistent gastro-intestinal fistulae, peritonitis, hepatitis, cirrhosis, ulcerative colitis, hyperthyroidism, malignant neoplasms. In any of the foregoing, the level of the protein may be conspicuous by its low state, but completely overlooked unless an estimation is made.

The symptoms of deficiency of protein do not stand out as an entity, but are submerged with other complaints and signs of the primary disease. There are some symptoms, however, which are indicative and suggestive of a low protein level, and it may be well to consider now the chronic type. Suppression of urine is not an infrequent accompaniment of many surgical conditions, and it has been shown that upon osmotic pressure the excretion of fluids is largely dependent. The lowered content of the albumin in the plasma is reflected in the renal function; and by re-establishing the level the excretion of water is greatly facilitated. The impairment of the liver function as the result of low proteins is now recognized. Gyorgy and Goldblatt[4] found that necrosis and cirrhosis of the liver were present in rats on a low protein diet, and it has been corroborated by other investigations, and the addition of metheonine to the diet would prevent the patholcgical changes in the liver. Beems and Endicott have applied the research in a series of clinical cases with a very favorable response. We are on the threshold of some important advances in hepatic disease largely related to protein.

One of the most striking effects of protein deficiency is the loss of body weight and strength. During the post-operative period the demand for protein is usually not satisfied either by the ingestion and assimilation of food or by parenteral fluids; consequently, the labile and dispensable reserves are drawn upon, as well as the stored sugars and fats. If the replacement is insufficient, loss of weight becomes an actuality although rarely is any attempt made to weigh the patient. The loss of weight following major operations varies from five to fifteen pounds. That proteins participate in the loss is incontrovertible as a determination of the nitrogen balance day by day will verify. We[3] have investigated and reported a series of cases where an accurate record was kept of the intake and output of protein and a negative balance was always present in our cases in major operations. One could be deceived by the mere maintenance of the patient's weight if scales were the only criterion of loss, because the liberal use of parenteral fluids, often with an excess of sodium chloride, leads to edema. Low plasma protein is often associated with accumulation of interstitial fluid, referred to as surgical edema. Under either of these conditions, a patient may show an increase in weight after an operation, but in a negative nitrogen balance. We should regard loss of weight as an invasion of the patient's reserve of protein. Swelling of the scrotum, edema of the face, hands, and back are early signs of surgical edema, but these are only the external or visible evidence. At the same time there is hidden edema in the muscles, the lungs, and even the heart may be involved.

The chronic surgical case often presents a nutritional problem, particularly in reference to protein; and it is well not to forget that every cell in the body contains some form of protein. Most of us can recall cases of persistent vomiting, incomplete intestinal obstruction, diarrhea, discharging fistulae, or malignant disease in which there has been a steady decline in the weight and strength of the patient that is not reflected in the routine hemogram or urinalysis. In such cases adequate laboratory examinations will demonstrate that a negative nitrogen balance is present and the plasma protein is approaching the critical level. We should alert ourselves to the possibilities in such cases, not that the downward trend can always be arrested, but at least an intelligent effort can be made in that direction.

Surgeons have been baffled and embarrassed by the disruption of abdominal incisions which had been closed with meticulous care in a routine manner. For no accountable reason the wounds open or disrupt with little or no evidence of healing about a week after the operation. It has been convenient and usual to place the blame on catgut, insecure knots, or acts of the patient, such as coughing,

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sneezing, or getting out of bed. The explanations were not convincing because the concepts were not in accord with facts. Ravdin was able to show beyond a reasonable doubt that most of the accidents occurred in animals in which there was a deficiency in protein, but the wounds healed promptly when adequate protein was given. Subsequent clinical experience corroborated Ravdin's work and now it is accepted by those qualified to judge that low protein level delays the healing of ulcers, bedsores and surgical wounds, irrespective of their location. Co Tui has convinced many that the healing of peptic ulcers can be accelerated by the use of amino acids, which is just another way of furnishing protein.

Many unexplained intra-abdominal surgical complications, such as leaking anastomosis, and obstruction, may be closely related to protein deficiency. How, then, shall the deficiency be met in the chronic case? We do not believe it is practical to run a nitrogen metabolism test on each patient, but the routine laboratory examinations plus a plasma protein level should be obtained in any case and at any time that the question of protein deficiency arises, and the decision will be based on a comprehensive history and a careful examination at such periods as our judgment would dictate. As noted under acute hypoproteinemia, blood transfusions have a place where more blood cells are needed, but aside from this we should depend on plasma and amino acids plus glucose parenterally, to which are added such alimentations that supply protein, carbohydrates, and fat that can be assimilated. We are so compelled for many reasons to rely on parenteral solutions to maintain nutrition and supply a reasonable number of calories, that our first thoughts turn to solutions infused directly into the circulation. The cost of plasma prohibits its use in large amounts or over a long period of time, although it is almost an ideal source of protein because it is utilized more rapidly than any other intravenous solution, and if properly prepared and given, is devoid of risk or reaction.

We are often compelled for obvious reasons to rely on parenteral solutions to maintain nutrition as well as to supply a sustaining number of calories, and there are at hand a variety of preparations for this purpose. The cost of plasma, at least until recently, prohibits its unlimited use, although it has the advantage of being rapidly utilized, has minimal reaction and may supply antibodies which could be a factor in combating infections. Just what protection or curative measures lie in the globulin of the plasma cannot be expressed in statistics, but enough evidence is at hand to believe it has a therapeutic value. Should it be asked how much plasma should be given at a single administration or how much daily, I would say that I do not know, but 20 c.c. for every kilo of body weight in 24 hours is not far wrong. A word of caution is necessary regarding the use of pooled plasma. Unless every single donor contributing to the pool is thoroughly screened, the danger of hepatitis cannot be ignored. It is better to use plasma from a single individual in which the possibility of hepatitis does not exist.

Garrott[6] and his associates, in a recent contribution to the therapy of hypoproteinemia, on the basis of the critical study of nine cases, found the protein concentration was most effectively altered by the administration of blood and plasma. He noted that while the level in the plasma was not always immediately elevated, the total plasma in the circulation showed a marked response. Though it was possible to maintain nitrogen balance, much protein introduced into the circulation through the use of blood and plasma could not be accounted for, and it was presumed that it was converted into tissue protein. Whipple originally proposed this explanation.

The response to any form of protein therapy may not be apparent in the plasma level, particularly in protracted illnesses; and impaired activity of the protein-forming mechanism residing in the liver could account for the delay, but the response is more rapid after blood and plasma than any other intravenous fluid.

They felt that whole blood added considerable protein through the hemoglobin and should especially be indicated even in mild anemia with low plasma protein. They conclude their contribution by stressing the generous use of blood and plasma and urge the necessity of increasing the available supply of both.

We have used most of the amino-acid solutions now offered to the profession; and, though we have our preference, most are satisfactory if given with the technical care the procedure rates and with observation of the patient during the administration. We have found that with amino-acids alone it is almost impossible to keep the patient in nitrogen equilibrium, and for that reason we have supplemented this form of therapy with glucose in salt

solution and glucose in distilled water. By this means it is possible to maintain a positive balance and supply adequate calories for a convalescent patient. It has been our practice following most major surgical cases, particularly those involving the gastro-intestinal tract, to give 1000 c.c. of amino-acid solution, 1000 c.c. of 5% glucose in saline, and 1000 c.c. of 5% glucose in 1000 c.c. of distilled water in the first and second post-operative twenty-four hours, gradually tapering off as the patient tolerates liquids. To this we frequently add vitamin B complex and vitamin C, not because there exists a clear indication for their use, but because parenteral fluids are deficient in vitamins, and no ill effects follow their use. There seems to be no formula or guide that has been generally adopted for the use of vitamins, but their use seems empirical, or rests on no firmer foundation than the fancy of the medical attendant.

Those patients in which some type of gastric or intestinal drainage has been employed, such as the Wangansteen, Canter, or Harris tube, over a period of hours or days, will need more than 3000 c.c. of fluid parenterally. Should the patient present evidence of serious protein deficiency, more active measures should be adopted, chiefly by increasing the amount of plasma. When the plasma level approaches 5 grams or less, no form of protein therapy is followed by an immediate response, but perseverance is the keynote of the treatment.

Bovine plasma is not a safe substitute for human plasma, and at this writing has no place in the therapy of protein deficiency. Concentrated albumin and globulin from human plasma almost eliminate themselves by reason of the expense of preparation and do not warrant much discussion as a routine therapeutic agent. No preparation of gelatin is equal to the amino-acid solutions in protein deficiency; gelatin contains very little available protein and it has been recommended chiefly to raise or maintain blood pressure in shock.

Several years ago we attempted to utilize ascitic fluid obtained from patients with hepatic cirrhosis as a substitute for plasma, visualizing it as a protein solution in abundant supply, but, first using it on animals, we found its effects unpredictable and sometimes alarming. Davis, who assisted us in this work, has continued the investigation and reports some satisfactory results, but it has not found much popularity.

We are in entire accord with Sir Berkeley Moynihan, when he said, "We have made surgery safe for the patient; now let us make the patient safe for surgery."

BIBLIOGRAPHY

1. Whipple, G. H.: *Surg., Gyn. and Obst.* **73**:886, 1941.
2. Ravdin, I. S.; Stengel, A., Jr., and Prushankin, M.: *J.A.M.A.* **114**:107, 1940.
3. White, Charles S.: *Medical Annals, D. C.* **XV**: No. 6, 251-259; June, 1946.
4. Gyorgy and Goldblatt: Editorial *J.A.M.A.;* April 3, 1948.
5. Whipple, G. H.: *Amer. Jour. Med. Sci.* **203**:477, 1942.
6. Garrott, A. J.; Bogardus, George; Egnes, Wellodene, and Phenister, D. E.: *Surg., Gyn. and Obst.* **86**:5; 604.
7. Miranda, Franciso deP.: *J.A.M.A.* **136**:542-545; February 21, 1948.

DISCUSSION

DR. CHARLES M. CARAVATI, Richmond: Dr. White has presented to us convincing evidence that low protein reserves are common in surgical disorders, particularly in post-operative states. He states that about one-sixth of the patients with cholecystitis and one-third of patients with uncomplicated peptic ulcer show low serum proteins upon admission.

The need for proteins in all surgical disorders is well known. Wound healing requires adequate available protein. Weight loss, which always occurs post-operatively, causes a reduction of serum protein, due to lessening of the blood volume.

To meet these requirements, adequate protein must be given: In order to raise tissue protein one gram, about 30 grams of serum protein must be formed. Therefore, large quantities of utilizable protein must be administered.

The oral route is always preferable. Restoration of normal serum levels are more readily accomplished in this manner than by the parenteral routes. Post-operatively, this may be given through the oro-jejunal tube, inserted at operation. Whole blood is the most effective intravenous substance to correct hypoproteinemia. Plasma and amino acids raise serum levels very little. You cannot maintain positive nitrogen balance by the giving of any known single protein.

It is important to emphasize that there is seldom a single deficiency. When protein stores are exhausted, there are usually other deficiencies such as vitamins and electrolytes. Most often when there is hypoproteinemia, post-operatively, there is also hypochloremia. Therefore, in planning substitution therapy, we should administer all substances which are deficient—replace proteins, chlorides, potassium, vitamins, blood and all other substances which may be inadequate.

I want to thank Dr. White for again emphasizing the importance of supplying protein to surgical patients. He has been one of the foremost advocates of the use of supplemental proteins in all types of surgical pathology and has had extensive experience with substitution protein therapy.

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THE EARLY DIAGNOSIS OF BRAIN TUMOR*

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Writers on the subject of brain tumor prior to 1900 and during the first two decades of this century emphasized the importance of early diagnosis but they had so little to offer in accurate localization and cure that the profession was not interested in a condition with such a dismal outlook. Even at the present time, with the results of surgical treatment of brain tumor comparing favorably with the results of treatment of other major tumors there is still much pessimism in the minds of some of the profession as to the benefit of surgical treatment of brain tumors or indeed of any intracranial lesion.

The diagnosis and treatment of brain tumors made no progress until the surgeon assumed responsibility for diagnosis, localization, operation and post-operative care, and ceased to function merely as the hands of the neurologists. In a discussion of brain tumors one naturally thinks of the monumental work of Sir Victor Horsley and Harvey Cushing, both of whom were pioneer neurophysiologists as well as neurological surgeons. Under Cushing the operative technic of brain tumors far out-stripped diagnosis but because of inaccurate diagnosis and localization many of the operative procedures consisted only of a subtemporal decompression for the relief of general pressure from a tumor with its location still unknown.

A patient with a brain tumor cannot be expected to make any material improvement unless the tumor is removed. Decompression for the relief of general pressure from tumor, while protecting vision and reducing headache, nevertheless accomplishes no lasting benefit. Early diagnosis of brain tumors with modern neurosurgical methods permits removal of the tumor before local pressure may cause permanent damage of adjacent areas of the brain or before generalized pressure results in impairment or loss of vision.

The progress made in the treatment of brain tumor during the last two decades is due in a large measure to the alertness of general practitioners, internists and ophthalmologists who have become brain tumor conscious and thus obtain early treatment for these cases. By merely suspecting a tumor, in the presence of chronic, progressive cerebral disturbance, there is sufficient conviction to have such studies made as will either verify or disprove a tumor.

A complete discussion of diagnosis in brain tumor would require a consideration of all that is known of cerebral physiology. Therefore, this discussion will be largely confined to general signs and symptoms which may lead to a suspicion of an intracranial neoplasm. The diagnosis of brain tumor is not a laboratory diagnosis, regardless of how many such studies are made. In most cases the physician will find himself, at the completion of many laboratory studies, about where he started.

At this point it may be well to speak of some of the studies and observations ordinarily used to determine whether a patient has an intracranial neoplasm. A careful clinical history and neurological examination are essential in every case of chronic cerebral disturbance. Clinical examination may give sufficient objective findings to warrant further study and tests to establish or rule out a suspected localized intracranial lesion.

Those who are interested in the subject of brain tumors, through their own experience and that of others, have learned to suspect brain tumor in the presence of certain simple and easily observed phenomena. As one of many examples, when a patient presents himself complaining of headache and during the consultation keeps one eye closed, a safe assumption is that he has double vision and closes one eye to prevent diplopia.

Many years ago when brain tumor was recognized only after the growth had produced tremendous intracranial pressure, the symptoms of brain tumor were listed as headache, choked discs and vomiting. All of these, when due to tumor, are late

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signs and symptoms of increased intracranial pressure due to obstruction of the cerebrospinal fluid circulation. Vomiting is usually a late symptom when due to tumor. It is not of much value in the diagnosis unless accompanied by persistent headache, for vomiting may be caused by so many other conditions. However, when severe headache from brain tumor is accompanied by hurried vomiting it is a sign of serious intracranial pressure such as may prove fatal unless promptly relieved. In young children with frequent unexplained vomiting, a neurological examination should be done with careful examination of the eye grounds. Nearly all patients with brain tumor causing other symptoms have headache, but headache alone without supporting signs is rarely an indication of brain tumor. Furthermore, since headache is one of the most common of human complaints and brain tumor is relatively rare compared with the number of headaches, a very small percentage of patients with headache have brain tumor. The observing physician will soon learn that headache of brain tumor differs from that of headache due to other conditions. For instance, the headache resulting from migraine is one of the most severe types but it has typical characteristics. Patients with brain tumor, even with choked discs, often complain little of headache unless asked about it, whereas, patients with functional headache will complain bitterly and incessantly and state it cannot be relieved by any treatment such patients have usually had. The headache of brain tumor usually can be relieved easily, at least temporarily. Often five or ten grains of aspirin will relieve such headache. Getting out of bed and walking around may relieve the headache. One will find that headache of brain tumor is usually worse in the morning after the patient has remained horizontal for some hours, increasing venous stasis in the brain and causing greater intracranial pressure. When there is sudden, violent headache in the occipital region in a patient with a history of chronic headache, one would suspect a sudden block of the ventricular system and should expect a fatal outcome unless the intracranial pressure is promptly relieved. The more severe a headache may be from tumor, the more dangerous it is to give opiates for relief. In such cases the severe intracranial pressure from the tumor is already impairing action of the center of respiration and administration of morphine or other opiates simply adds to the embarrassment of the already compromised respiratory center. While headache is present in a great majority of brain tumor cases by the time the physician is consulted, some patients with large tumors have no complaint of headache at any time during the course of the disease. It is probable that unless the tumor is attached to the parietal dura or unless it is causing ventricular obstruction, headache will not be a chief complaint. The location of headache in brain tumor is of little value in the localization of the lesion.

Choking of the optic discs is an objective finding of greatest importance in the study of intracranial lesions. In the early years of brain tumor surgery it was considered necessary to find choked discs before one would agree to the diagnosis of brain tumor. Modern diagnosis often requires the recognition of tumor before the development of papilledema. There are two main effects of brain tumor: first, the local effects or impairment of function of cerebral structures in contact with the tumor; second, generalized increased intracranial pressure. It is highly desirable to recognize the presence of tumor and its location before permanent damage is done locally or to vision by intracranial pressure.

A tumor of the motor cortex, which is one of the easiest of all to diagnose, should be strongly suspected and in many cases diagnosed by its local cerebral effects, such as Jacksonian convulsions with progressive weakness of the extremity involved. Another easily recognized lesion is that of tumor of the pituitary which should be detected before the patient becomes blind from pressure on the optic chiasm. Tumor of the motor area and pituitary are practically self-localizing and announce their presence by characteristic clinical signs and symptoms. If a tumor in the motor area is allowed to grow, the patient will usually develop choked discs in addition to paralysis of the contralateral extremities.

It is well to remember that objective findings are of greater importance than subjective complaints in the study of brain tumor. Choked discs or visual field defects, progressive loss of sensory and motor function on one side, or Jacksonian attacks are so clear cut there should be no doubt of the presence of a cerebral lesion.

Unlike tumors, such as cancer, in other parts of the body, malignant tumors of the brain do not become inoperable primarily because of the length

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of time they have existed. On the other hand, cancer of the breast, stomach or bowel becomes inoperable at a certain time, due to extensive metastases. Tumors of the brain do not metastasize. While the brain tumor may not become inoperable, complete removal is not always possible as in extensive infiltrating gliomas. Moreover, there are certain inoperable brain tumors because of location. Among these are pontine tumors and infiltrating tumors of the left motor and speech areas.

The importance of X-ray examination in the diagnosis of cranial and intracranial lesions is well recognized. However, there are not many instances in which plain skull films will disclose a tumor although it may be suggested by certain secondary changes in the skull. In late cases, convolutional impressions, thinning of the skull and separation of sutures in children are frequently seen on films from high intracranial pressure. X-ray study of the skull in pituitary tumors gives most important information. In these cases the sella turcica is enlarged and there are generally some erosive changes in the walls of the sella. In some meningiomas, a very common benign tumor of the brain, there are very often bone changes with enlargement of the blood vessel grooves of the skull overlying the tumor. In tumors of the cerebellopontine angle there is frequently enlargement of the internal auditory meatus with erosion of the petrous portion of the temporal bone. In certain rare cases there may be calcification in the tumor which will be demonstrated on X-ray films. When the pineal body is calcified, as it is normally in a large percentage of adults, considerable information can be gained as to whether it occupies its normal midline position or whether it is shifted away from the side of a mass lesion by local pressure. In the vast majority of early cases, however, plain X-ray films will not give the information desired, particularly as to the location of the tumor. In many cases, X-ray films of the chest prove of more value in the diagnosis of brain tumor than X-ray examination of the skull. It is routine in our clinic in the study of brain tumor to make X-ray plates of the chest in every adult patient. We insist on this even when physical examination of the chest by the internist has disclosed no signs of pathology. If a tumor of the lung is disclosed in the presence of marked cerebral symptoms, then one may often conclude there are metastases in the brain.

Brain surgery became an established specialty only after the development of ventriculography by Dandy in 1918. This is the most valuable contribution yet made not only to the diagnosis of brain tumor but to cerebral surgery as a whole. The authors believe there are two outstanding and most important contributions to the diagnosis and treatment of brain tumors: (1) the meticulous closure of the operative wound which Cushing emphasized and practiced, (2) precise localization of the tumor by air studies as developed by Dandy. Tumors of the brain could not be treated successfully in the absence of either.

A few years before Dandy developed ventriculography, Von Eiselberg stated there were only two kinds of brain tumor that were operable—those which were made manifest by Jacksonian attacks, therefore were in the motor area, and those of the pituitary in which there was visual impairment and the X-ray films showed enlargement of the sella. With modern diagnosis it is possible to locate, operate and remove tumors successfully in practically every part of the brain.

It is difficult for one entering brain surgery since Dandy's contribution to appreciate the uncertainty and discouragement of surgery of brain tumors prior to that time. There were brilliant medical neurologists but it was impossible for them by clinical study alone to make accurate localization. Many tumors removed today could not be diagnosed nor even suspected when relying on neurological study without air injection. The more experience one has in the diagnosis of brain tumor, the more he realizes the value of air studies for precise localization. With such information it is possible to make a direct approach, therefore requiring a much smaller exploration. Even so, the value of air injection has by no means excluded the importance of careful clinical study of the patient as a primary part of the examination. Unless clinical study indicates the need of ventriculography, obviously it should not be done. Air injection, or any other operative procedure no matter how minor it appears, is not without some danger. If ventriculography or encephalography shows no evidence of tumor or other space restricting lesion, the danger of the test is extremely slight, but if the films show a tumor, then immediate operation is demanded. With proper clinical study, supplemented by air injection, the diagnosis of brain tumor is about as accurate as

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diagnosis of lesions of the kidney in which there are also mechanical aids to diagnosis.

The profession generally thinks of brain tumor as a slowly developing lesion with symptoms that also develop slowly. This is usually the case, but there are cases of brain tumor (about 25%) that manifest themselves in an explosive manner, simulating the sudden onset of symptoms of a cerebrovascular accident. For instance, a tumor in the ventricle, due to suddden change of posture, may block the ventricle and produce immediate symptoms not unlike that of an apoplectic stroke. The walls of blood vessels of rapidly growing brain tumors are fragile and may rupture, giving rise to sudden onset of symptoms by enlargement of the tumor. In some cases a patient may develop sudden symptoms from thrombosis of one of the large vessels in the cerebral hemisphere. The result may be extensive softening of the brain with edema, and displacement of the structures to the opposite side of the skull. Air injection in such a case may not differentiate between thrombosis and tumor but in either case operation should be done. Air studies should be made in all cases where there is only a slight possibility of tumor.

A patient may have a brain tumor for years and suddenly develop symptoms from rapidly increasing cerebral edema caused by the tumor acting as a foreign body in the brain tissues. We have seen this in a number of cases in which the tumor was small and did not block cerebrospinal fluid circulation but the hemisphere in which the lesion was located was edematous and greatly enlarged as compared with the other side.

Convulsions have their greatest frequency in children, and ordinarily these convulsions are not due to an intracranial neoplasm. The attacks do have a definite underlying pathology which is often atrophy or scarring of the brain as shown by air injection. In these cases, in which intracranial pressure is not high, a spinal air injection is done. When convulsions develop after the age of 25, with no history of head injury, brain tumor should be suspected. Ventriculography or encephalography is indicated in every such case.

Blood pressure observations give little information in the study of brain tumor. As a rule the blood pressure tends to be lower than normal except at such times as the intracranial pressure is suddenly raised. Lumbar puncture has little value in the diagnosis of brain tumor, and in cases showing signs of increased intracranial pressure this procedure is positively dangerous. Withdrawal of fluid at lumbar puncture when a brain tumor is causing high intracranial tension may cause herniation of the cerebellar lobes into the foramen magnum, compressing the medulla, often with a rapidly fatal result.

Electroencephalography has received considerable attention from those interested in cerebral disease. We have not used it in brain tumor cases nor would we rely on its findings without supplementary encephalography or ventriculography. In competent hands and with expert interpretation, it is valuable in the study of convulsions.

SUMMARY

The following brief summary is made to give added emphasis to certain points in the paper:

(1) The diagnosis of brain tumor requires answers to the following questions: (a) Is there a tumor? (b) If so, what is the location? (c) What is the type of tumor.

The answer to the third question is being made with increasing frequency before operation but still with far more uncertainty than the answers to the first two questions.

(2) Brain tumor should be suspected in any case showing chronic, progressive cerebral disturbance not adequately explained on some other basis.

(3) About 25% of brain tumors show sudden onset of symptoms similar to that of vascular lesions. Differentiation can be made only by air injection in many cases and, if there is any doubt, a ventriculogram should always be made.

(4) Relatively few tumors can be diagnosed and localized by clinical study and x-ray examination alone. If there is reasonable suspicion of tumor from the clinical studies, ventriculography is always indicated.

(5) In many cases in which the surgeon is reasonably certain of the diagnosis and location of brain tumor, air studies are still indicated for precise localization to permit more direct surgical approach to the tumor.

DISCUSSION

DR. W. GAYLE CRUTCHFIELD, Charlottesville: I am always pleased to hear Dr. Coleman speak, and I am glad to be here this morning although there is very little, if anything, I can add to what he has said.

The mortality from brain tumor operations is between

ten and fifteen per cent, perhaps closer to ten per cent. This could be greatly reduced by earlier hospitalization, as pointed out by Dr. Coleman, also by proceeding with the operation just as quickly as possible after the patient is admitted to the hospital.

The mortality and morbidity of brain tumor cases awaiting operation in hospitals are not a matter of record insofar as I know, but I am reasonably certain that they would reach a substantial figure. Not infrequently, the patient who is being subjected to routine studies and who does not appear to be in immediate danger suddenly develops respiratory paralysis or becomes deeply comatose. If in such cases immediate operation is feasible, it is usually fraught with many difficulties and it seldom meets with much success. To cope with situations such as this, I believe all of us should regard these cases as emergencies and proceed with surgical treatment at the earliest possible moment.

It is very depressing to see patients with irreparable loss of vision due to increased intracranial pressure, particularly since so many of these patients harbor a benign growth. So many of the malignant tumors progress so rapidly that the patient's life is lost, or there is obvious evidence of serious disturbance of function before secondary optic atrophy reaches a serious degree. Loss of vision is usually gradual; therefore, the early, or even reasonably early, recognition of a brain tumor should prevent complete loss of vision.

Drug Raises Mental Age.

Encouraging evidence that children born with mongolism, one of the most serious and least understood forms of mental deficiency, may no longer be doomed to idiocy or imbecility is reported by researchers.

Mongolism takes the largest toll of all abnormal prenatal conditions among the normal population of the United States, according to medical authorities. About three out of every thousand babies born in a general lying-in hospital in this country are affected. Mongoloid babies are especially lively and imitative and have characteristic slanting eyes, flattened skull, and short thumbs and little fingers.

In seven of these children, mental development has been significantly accelerated by doses of glutamic acid, one of the chemical compounds known as amino acids which are building blocks for cells of the body, Drs. Frederic T. Zimmerman and Bessie B. Burgemeister, New York, and Dr. Tracy J. Putnam, Beverly Hills, Calif., write in a current issue of *Archives of Neurology and Psychiatry*, published by the American Medical Association.

Glutamic acid is simple to administer and is generally available to doctors.

"The average mental age of our group of children with mongolism was raised from three years six months to four years two months, or a gain of eight months in the six-month treatment period. This is higher than the rate of growth expected of children having average intelligence (six months in a six-month period) and more than twice the previous rate of mental development of the group."

These seven children are only a small number of a large group of mongoloid patients now receiving glutamic acid, and the doctors do not know yet whether all mongoloid children can be helped by the drug. Pathologic changes in the spinal cord are known to be present in some mongoloid children, and may be the cause of the condition. The amount of potential mental improvement of each child appears to depend on the degree to which the nervous system has been damaged, the doctors say. Experiments have indicated that glutamic acid acts as a stimulant to production of impulses by the nervous system. The learning process takes place through these impulses.

RECENT ADVANCES IN CATARACT SURGERY*

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Roanoke, Virginia.

Cataract surgery has undergone a gradual evolution in the last twenty years with the great increase in popularity of intracapsular extraction. The advantages of removing the intact capsule are unquestionable and should be evaluated not only in terms of improved visual results, but in terms of sparing the patient the psychic trauma and possible economic uselessness of years of increasing darkness while he waits for the cortex to mature sufficiently for an extracapsular operation. The evolution from the extracapsular to the intracapsular method had its real beginning in the work of Col. Henry Smith of the British Indian Service. In 1903, Smith published a report of 6,500 cataract operations in which he had secured very good results by expressing the intact capsule by external pressure alone. Despite the many advantages of the intracapsular method and the excellent results obtained, there are many good ophthalmic surgeons who continue to do the extracapsular operation. Among the advantages of the intracapsular method: 1st: Can be done without waiting for the cortex to mature. 2nd: Complications, such as iritis and iridocyclitis, and glaucoma are less likely to develop. 3rd: Retained cortical material is always a potential danger.

It is possible to remove the lens from the eye without loss of vitreous because the zonular fibers, which attach to and support the lens, are independent of the hyaloid membrane of the vitreous and

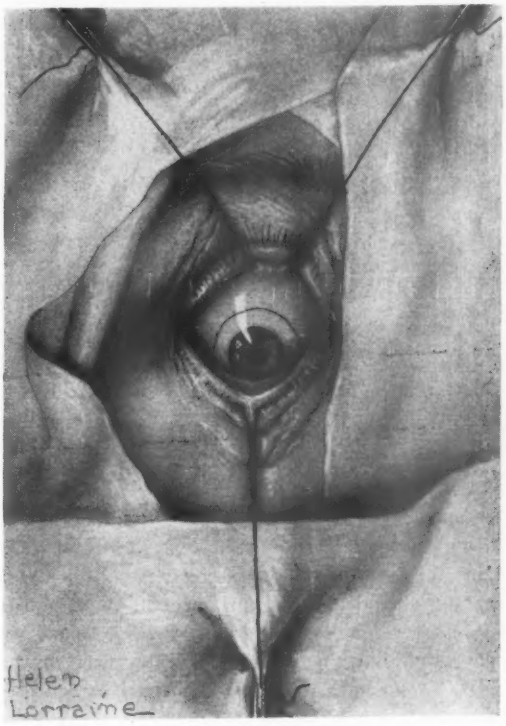

Fig. 1. The position of sutures for retracting the lids, and the conjunctival incision.

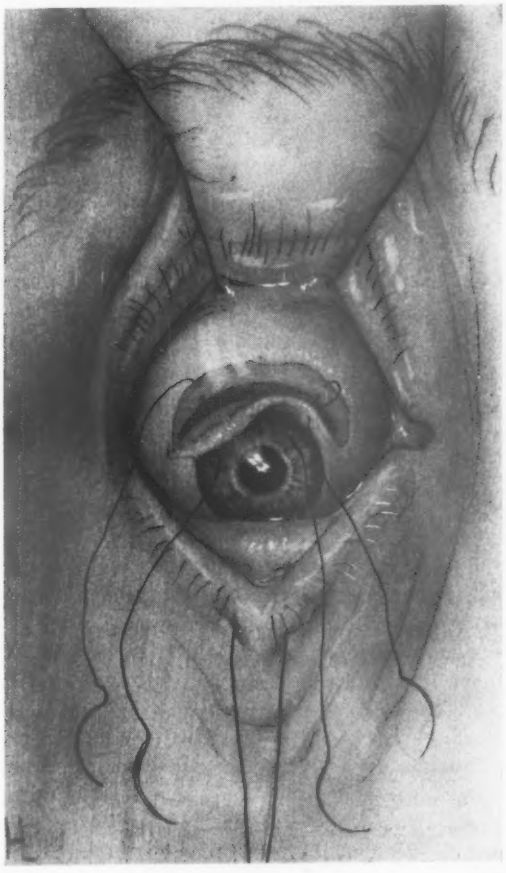

Fig. 2. Sutures placed in cornea.

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can thus be ruptured without a resultant rupture of the hyaloid membrane, and because these zonular fibers do not come into contact with the ciliary processes except in their posterior portions, whereas it is at their capsular insertion that they are ruptured in extracting the lens. These fibers are weakest at the point of their capsular insertion and become more weakened with advancing age. Age also

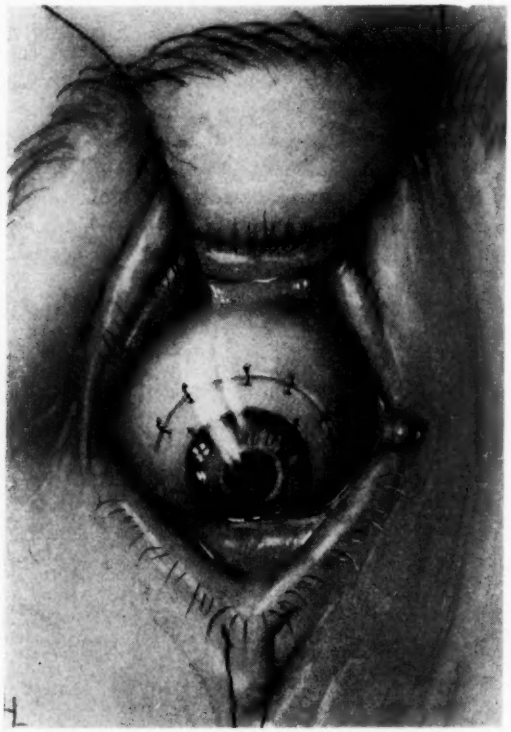

Fig. 3. Corneo-scleral sutures tied on the corneal surface 10 o'clock and 2 o'clock, and also the conjunctival sutures.

has the effect of thickening the capsule and loosening the adhesion between the capsule of the lens and the hyaloid membrane; hence, the particular indication of intracapsular surgery as the procedure of choice in senile cataracts. In young persons the suspensory fibers are generally so elastic as to make subluxation of the lens impossible.

All methods of lens delivery are based upon one of three principles: (1) external pressure alone, (2) subluxation with forceps plus some degree of external pressure, and (3) suction. Procedures also vary as to whether the lens is delivered head first or by tumbling. The tumbling technic consists of rupturing the lower zonular fibers first and applying pressure in such a line as to cause the lower pole of the lens to present in the wound first.

Pressure delivery is based upon the principle that pressure applied to liquid in a distensible sac is transmitted equally in all directions. Smith's original technic utilized external pressure alone to effect either a head on or a tumbling delivery. The technic which we use in our clinic has been worked out by picking up a little bit here and a little bit there and by constantly endeavoring to utilize the best

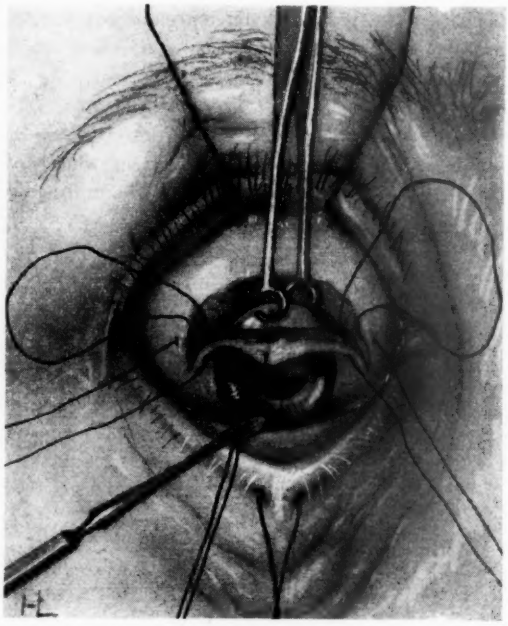

Fig. 4. The method of applying Verhoeff capsule forceps to the equator of the lens just as it presents in the wound. The central suture is used for traction and this gives the operator a direct view of the lens. Capsule forceps are applied accurately and deliberately.

features of any procedure. It is the result, not only of our own experience in operating, but of observations in eye clinics in various parts of this country and abroad and of experience gained in assisting operators, from the various medical centers, at our hospital during the past twenty years in the week of our spring graduate course. Our goal is to remove the cataract in such a way as to cause the least possible disturbance of the functions of the eye and to give the patient useful and serviceable vision. Although we give careful attention to such things as proper diagnosis, a thorough physical examination, and necessary preoperative care, including the elimination of foci of infection, we have

found that more depends upon the operative technic than upon the patient's general condition or the type of cataract involved. We have noted that postoperative complications have been reduced in direct ratio to our improvement in surgical technic. The following procedure is now giving us uniformly good results.

TECHNIC

The patient is admitted to the hospital one day prior to the operation and, after a complete physical examination, is given a mild sedative and a soapsuds enema. As safeguards against infection the lachrymal sacs are irrigated the night before operation with a one to ten thousand solution of penicillin, and after the patient is on the operating table just prior to the operation, one drop of 1 per cent silver nitrate is instilled into the eye and immediately washed out. Occasionally we give 20,000 units of penicillin intramuscularly every three hours for twenty-four hours prior to operation. The decision as to whether an iridectomy will be performed is made before the patient comes to the operating room and depends upon whether or not the pupil dilates readily. We dilate the pupil by the method which Koke has described. If it responds readily, we preserve the round pupil, but if it does not, we perform a full iridectomy. One hour before the operation we give an hyoscine, morphine, cactine tablet hypodermically, and 1½ grains of "nembutal" by mouth. Then the dilatation is begun by instilling two drops of 0.2 per cent scopolamine hydrobromide in the cornea. Thirty minutes later two drops of 0.5 per cent pontocaine hydrochloride are instilled and are followed in two minutes by one drop of 10 per cent "neosynephrine" hydrochloride. After the patient is taken to the operating room, the first instillation of 5 per cent cocaine is made, and two minutes later one drop of "neosynephrine" is placed on the cornea. Approximately fifteen minutes later local anesthesia is completed. If we suspect that the patient may be difficult to handle, a retrobulbar injection of 0.5 c. c. of 1 per cent solution of procaine with epinephrine is made. Akinesia is produced by the van Lint method.

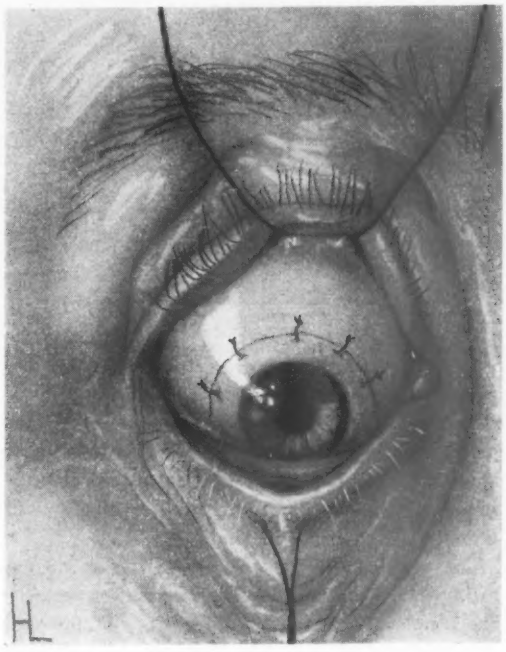

Fig. 5. The method of closing the conjunctival incision. As many sutures can be used as necessary to completely close the wound.

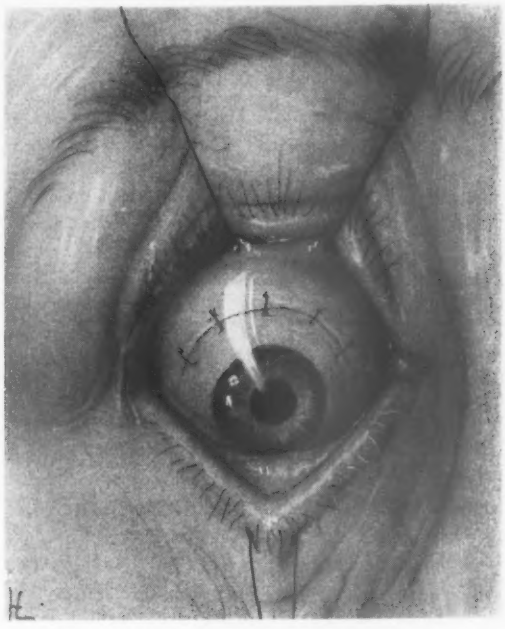

Fig. 6. Wound closed and round pupil.

We do not use a lid speculum, but hold the lids open and the eye down with silk sutures. The upper suture is placed under the superior rectus muscle 4 to 6 mm. back of its insertion. Care is taken not to place it too close to the insertion of the tendon as this makes too much traction upon the globe.

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The lower lid is held down by a suture placed through the skin near the lid margin. The sutures are attached to the drapes by hemostats. With the speculum eliminated in this way the eye may be closed quickly and easily in case the need arises, and there is no traction on the globe so that the possibility of loss of vitreous is minimized.

The next step is the formation of the conjunctival flap which is 3 mm. from the corneal limbus and extends a full 180 degrees concentric with the limbus. The dissection is carried out very carefully and deliberately to avoid buttonholing and includes not only the conjunctiva but episcleral tissues as well. The conjunctiva is grasped with toothless forceps.

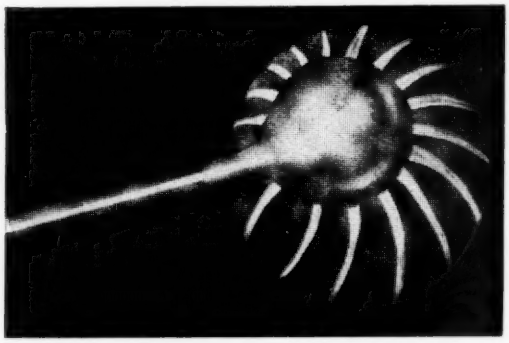

Fig. 7. Suction tip in place on lens capsule, showing lines of stress. (After Thomas, (*Archives of Ophthalmology*, 39, June, 1948.)

All bleeding points are carefully controlled either with epinephrine or by touching the bleeding points with the end of a strabismus hook which has been heated in the flame of an alcohol lamp.

Cornea scleral sutures are placed by using a double-armed number 6-0 silk on atraumatic needles at 10:00 o'clock and 2:00 o'clock. One needle goes through the sclera, conjunctiva, and cornea. The other only goes through the conjunctiva. The sutures are placed before making the keratome incision.

Conjunctival sutures are placed at 10, 12, and 2 o'clock. The two lateral sutures go through both edges of the conjunctiva and are looped out of the way. The central suture does not go through the upper flap of the conjunctiva and is used for traction by the assistant during the iridectomy and the extraction of the lens.

A conjunctival flap of the size used makes an incision with the knife unhandy; so, following the technic described by Cooper. we make a keratome incision. The point of the keratome goes through at the limbus and extends the full width of the cutting edge. We have a specially devised keratome which is 14 mm. in width at its base. The incision is widened with scissors. By repeated small snips the incision is enlarged to the horizontal meridian. The scissors guide the incision and the possibility of injuring the iris is thus eliminated.

If an iridectomy has been decided upon, it is performed at this point. The assistant makes slight traction on the central suture, thus bringing the iris clearly into view. The iris is grasped near the

Fig. 8. Capsule forceps in place on the lens capsule, showing lines of stress. (After Thomas, *Archives of Ophthalmology*, 39, June, 1948.)

pupillary border and the iridectomy is performed. The angles of the coloboma are then carefully inspected and placed in good position with an iris repositor. If at any time blood enters the anterior chamber, it should be washed out immediately with penicillin solution 1-10,000.

The final step in the operation is the extraction of the lens in capsule. We use the head on method. The zonular fibers are ruptured by point pressure at 4 o'clock, 6 o'clock, and 8 o'clock. We also lift the cornea by traction on the central suture and go inside the anterior chamber with a very small iris repositor and make gentle pressure on the iris at 3 o'clock and 9 o'clock. Firm continuous pressure is made on the limbus at 6 o'clock. The pressure is very slow, careful, and deliberate, and is never released. The moment the lens begins to present in the wound it is straddled with Verhoeff capsule forceps and delivered by manipulation and continuous pressure from below.

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As soon as the lens is delivered, the corneoscleral sutures are gently tied on the corneal surface. Care is taken to avoid the use of too much pressure. The two lateral conjunctival sutures are tied, and the iris is again inspected. The central conjunctival suture is then placed in the distal flap and tied. Additional sutures can be placed in the conjunctiva if necessary to close the wound completely. Care is taken to cover the incision completely as a safeguard against infection. If for any reason irrigation of the anterior chamber is necessary, it can be carried out under the flap. The sutures are removed on the tenth day.

After the wound is securely closed, the sutures in the lower lid and the superior rectus muscle are removed, and 1 per cent atropine is instilled in the conjunctival sac. We routinely use atropine rather than eserine because we consider keeping the pupil well dilated an additional safeguard against prolapse of the iris when the anterior chamber reforms. When the aqueous comes forward, it does not sweep the iris with it if the pupil is well dilated. We also find that with atropine there is less pain immediately following the operation.

Only the operated eye is bandaged, and if everything goes well, we allow the bandage to remain forty-eight hours before dressing the wound again. If pain occurs within twenty-four hours following the operation and is not relieved by a mild sedative such as empirin compound, the eye is dressed immediately and every twenty-four hours thereafter. The patient is placed in bed at an angle of from thirty to forty-five degrees. This practice has greatly relieved post-operative restlessness. A very distressing symptom immediately following the operation is backache. This can be greatly alleviated by a preoperative enema, a well cushioned operating table, a comfortable bed with an adjustable back rest, and the early and frequent turning of the patient in bed. The operative eye should be protected with a shield for at least twenty days to prevent possible injury. We usually allow the patient out of bed at the end of twenty-four hours, and if he becomes restless, we let him up the first day. We prefer that he be comfortable out of bed rather than uncomfortable in bed. The average period of stay in the hospital is about eight days.

ADVANTAGES

The four principal advances in surgery embodied in this procedure are: the elimination of the lid speculum, the full 180-degree conjunctival flap, the keratome incision, and the combination of conjunctival and corneoscleral sutures. The following are some of the advantages of the technic described.

(1) The eye can be closed quickly if necessary since an eye speculum is not used.

(2) The elimination of the eye speculum minimizes the possibility of the loss of vitreous since there is no pressure on the globe. With this complication lessened, the operator is more at ease. Calmness at all times is conducive to best results.

(3) The incision with the keratome can be made accurately, and there is no reason for injuring the iris, lens, or cornea. The incision heals just as efficiently and promptly when enlarged with scissors as with a knife. The scissors guide the incision, and the iris is not disturbed.

(4) We are always assured of a conjunctival flap of the proper width extending a full length of the incision. A conjunctival flap extending a full length of the incision is impossible with a knife, even in the hands of the most skilled operator.

(5) In our experience astigmatism has been one-fourth to one-half less with this type of incision than with the Graefe knife incision.

(6) Using the central suture for traction permits the iris to be brought clearly into view and, if an iridectomy is decided upon, it can be done carefully and deliberately and the coloboma can be thoroughly inspected.

(7) The use of the traction suture permits the lens to be seen the moment it presents in the wound. The Verhoeff capsule forceps can be placed accurately and deliberately so that the lens is grasped at the equator. According to measurements by Salzmann, the thickest part of the capsule is nearest the equator and the thinnest near the lower pole.

(8) The combination of sutures gives a firmly closed wound which acts as a safeguard against infection and possible prolapse of the iris. It also permits us to get our patients out of bed early, which is the best preventive of such general complications as hypostatic pneumonia.

(9) The preliminary sedation and thorough local anesthesia, in our opinion, give the patient the benefit of the greatest possible safety plus comfort. A good surgeon as a rule dislikes to put a patient to sleep if the operation can be carried out successfully with local anesthesia. Some ophthalmic surgeons are using sodium "pentothal" with good

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results, but the procedure requires the assistance of a trained anesthetist and is not practical for the occasional operator who does not have the benefit of such assistance. In addition, we prefer not to face the possibility, however slight, of the patient's being susceptible to the drug.

POSSIBLE COMPLICATIONS

Delayed Closure of Wound—We have not had a single case with our present use of the conjunctival flap.

Hemorrhages—We have had no expulsive hemorrhages in 300 cases. Anterior chamber hemorrhage, in my opinion, is due largely to two factors: (1) a faulty, jagged, irregular incision which delays healing and stimulates many new formed capillaries in the wound which rupture easily, and (2) failure to provide a firm conjunctival flap covering the entire incision. Since we adopted our present technic of keratome incision, conjunctival flap, and sutures, the incidence of hemorrhages has fallen to 3 per cent. Formerly it was as high as 15 per cent. Technic is of greater value in controlling this complication than the general condition of the patient. This observation is in conformity with the findings of Owens and Hughes in 2,086 extractions.

Iritis and Iridocyclitis—In my opinion these are largely due to retained lens material and are rarely seen following intracapsular extractions. If they do occur, we treat them, first, by desensitization to lens protein as recommended by Burky and Henton, and, second, by intravenous use of typhoid H antigen.

Prolapse of Iris—We have not had a case of iris prolapse in 100 patients operated upon since we adopted our present technic of dilating the pupil before and after operation and closing the wound with a combination of sutures. I agree with Stanley Smith and other authors that corneoscleral sutures are an important factor in preventing this complication, but I think that the dilatation of the pupil is of equal importance.

Glaucoma—Secondary glaucoma is closely associated with cases of iridocyclitis, loss of vitreous, and retained cortical material, and rarely occurs with present day technic. If it is not controlled with miotics, we do an iris inclusion operation.

SUMMARY

We use local anesthesia, van Lint akinesia, a keratome incision widened to 180 degrees with scissors, a combination of two corneoscleral sutures, and a 180-degree conjunctival flap closed by additional sutures. We hold the lids open and the eye down with silk sutures, and deliver the lens by the head on method. The patient is allowed out of bed twenty-four hours after operation. With this technic we have achieved a visual acuity of 20/25 or better in 90 per cent of cases: we have reduced hemorrhage to 3 per cent and vitreous loss to 2 per cent. We emphasize that this operation is not designed for speed but for safety and accuracy.

BIBLIOGRAPHY

1. Smith, H.: Extraction of Cataract in the Capsule. *Brit. M. J.* **2**:719, 1903.
2. Knapp, Arnold: Present State of the Intracapsular Cataract Operation. *Arch. Ophth.* **38**:1-38 (July), 1947.
3. Smith, H.: New Technique for Expression of Cataractous Lens in Capsule. *Arch. Ophth.* **55**:213 (May), 1926.
4. Stanculeanu, G.: Intrakapsulare Staroperationen. *Klin. Monatsbl. f. Augenh.* **1**:527, 1912.
5. Verhoeff, F. H.: New Operation for Removing Cataracts with Their Capsules. *Tr. Am. Ophth. Soc.* **25**:54, 1927.
6. Hulen, V. H.: A New Operation for the Extraction of a Cataract in Its Capsule. *Ophth. Rec.* **19**:651 (December), 1910.
7. Barraquer, L.: Phacoerisis. *Arch. Ophth.* **51**:488 (September), 1922.
8. Nugent, Oscar B.: Cataract Extraction by the Vacuum Method. *Illinois M. J.* **91**:243-48 (May), 1947.
9. Koke, M. P.: Ciliary Dilation and Vitreous Recession in Cataract Extraction. *Am. J. Ophth.* **30**:327 (March), 1947.
10. Arruga, H.: Failures and Complications in the Cataract Operation. *Ophth. iber. amer.* (B. Air.) **7**: 281-86, No. 4, 1946.
11. Cooper, F. Maxey: Easier and Safer Cataract Extractions. *Sou. Med. Jour.* **34**:698 (July), 1941.
12. Thomas, George J., and McCaslin, Murray F.: Pentothal Sodium in Ophthalmic Surgery. *Arch. Ophth.* **37**:452-58 (April), 1947.
    Reynolds, James S.: Cataract Extraction Under Sodium Pentothal. *Minnesota Med.* **29**:700 (July), 1946.
13. Owens, William Councilman, and Hughes, William F.: Intraocular Hemorrhage in Cataract Extraction. *Arch. Ophth.* **37**:561-71 (May), 1947.
14. Smith, Stanley C.: Early Ambulation of Post-Operative Cataract Patients. *Texas J. M.* **43**:183-86 (July), 1946.
15. Gill, Elbyrne G.: Cataract Surgery: Recent Advances. *Southern Medical Journal* **41**, No. 3 (March), 1948.

DISCUSSION

DR. EDWIN W. BURTON, Charlottesville: Dr. Gill was kind enough to send me a copy of his paper for reading before the meeting. I am heartily in accord with many of the points which he has suggested as a means of reducing the dangers and improving the results of cataract surgery.

That the intracapsular method of cataract extraction is the method of choice in most cases is now generally agreed. The post-operative reaction of the eye is decidedly less marked, secondary glaucoma due to retained capsular remnants never occurs, and the necessity for the patient to return for a discission later, requiring additional days of hospitalization, is avoided. The operation is more difficult to perform, but the results, optically, appear to be better. The intracapsular operation is now performed on younger subjects than when the operation first became popular. Although the zonular fibers are more resistant in the young, intracapsular extractions are now successfully performed in many of these cases. I wish that Dr. Gill had gone into more detail regarding the types of cases in which the intracapsular operation is indicated and the types in which it would be difficult or impossible to execute. Immature cataracts, the capsule of which can be firmly and securely grasped with the capsule forceps, are ideally suited to the intracapsular operation. Extraction of cataract after an iridocyclitis, with its thickened capsule, likewise is usually best accomplished by this procedure. On the other hand, the swollen intumescent cataract, with tense capsule, and the hypermature cataract with its slippery capsule makes intracapsular extraction more difficult. An extremely large nucleus, with little cortex likewise prevents a good grasp with the forceps.

I prefer tumbling of the lens to the head first method because it is easier for me to perform with a round pupil, and because by this method the zonular fibers are drawn tense at the point at which the counter pressure is made. If the forceps are held too loosely, they will slip off the capsule and if held too tightly, the capsule will be pinched and torn. If the blades do not close in perfect apposition, or if flaws are present, they cannot perform their function perfectly.

It is surprising how slowly corneal sutures have come into vogue, although they were occasionally employed by various surgeons a number of years before Kalt described his suture in 1894. I personally prefer the pre-placed suture according to the McLean or similar technique. A good bite can be taken in the sclero-cornea, and the wound is closed in perfect apposition. Sclero-conjunctival sutures do not afford protection to the same degree.

Hemorrhage into the anterior chambers appears to occur less frequently when a peripheral iridectomy is done than when a complete iridectomy is done, although the formation of newly formed capillaries in the wound is an important cause, as Dr. Gill states. Also with a round pupillar vitreous loss is less frequent because the intact iris diaphragm tends to hold the vitreous back.

The superior rectus suture, first used by Elschnig in the intracapsular operation, represents a great advance. It affords the operation a control of the globe not possible by any other means.

The use of the knife or keratome must rest with the individual surgeon. The keratome has been used for many years in making cataract sections. I still prefer the Graefe section.

I want to commend Dr. Gill for bringing to our attention these important points in regard to cataract surgery. It would not be correct to say that all of them are recent; whether some of the points are "advances" might also be questioned. In his hands his technique has been satisfactory. I wish that more detailed statistics had been included in his paper so that results and complications according to his technique could be compared with other series of statistics which have been published during the past several years.

DR. R. S. FARIS, Richmond: I want to take issue with the two gentlemen who have just spoken. Each of them said that this paper would not be of interest to general practitioners. I happen to be one of that group, and I want to inform them right now that the paper was tremendously interesting to me. Very often, I think, we general practitioners see the cataracts first; and it may be that if the specialists will instruct us, as these gentlemen have this morning, we shall become better doctors. I wish the paper could have been read before the entire group. Many of us are interested in seeing how this thing is done. I, for one, did not know before; and I want to thank you for presenting it.

DR. GILL, closing the discussion: I wish to thank both the discussants. I felt almost like apologizing for bringing a technical paper of this nature before a group of general men.

As to the particular technique that a surgeon uses, it is largely a matter of personal equation. Our goal is to remove the cataract with the least possible trauma to the structures of the eye and to give the patient useful vision. If that goal is attained the patient can resume his vocation in life if he is in a physical condition to do so.

I am very happy that Dr. Faris had a kind word to say on behalf of the specialists. I would have gone into more detail if I had thought the men in general practice would have been interested. Blindness, from the result of a cataract, is a great economic factor, and I think it is well for the general practitioner to know what it means, and, also, the patient who has the cataract. They should know that it can be removed with the modern technique without a great amount of shock to the patient, and that the hospital stay is about eight days, and the patient does not have to be in bed more than 24 hours after the operation.

I wish again to thank both men for the discussion of the paper, and the program committee for allowing us to bring a technical paper of this nature before the general practitioners.

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THE TREATMENT OF MALIGNANT MELANOMA*

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The adjective "malignant" could be omitted from the title of this paper for present usage of the term melanoma pre-supposes a malignant tumor composed of melanin-pigmented cells. A benign pigmented tumor is called a nevus pigmentosus. So malignant are all melanomas, however, that I welcome the opportunity to emphasize it in my title.

The mortality in this condition is always high. Pack[1] in 1947 analyzed 595 cases of melanoma which had been followed over a five year period at the Memorial Hospital in New York City. Only 9.7 per cent survived. This is a terrific mortality, especially when it is considered that these tumors almost always arise on the skin where they can be detected in their incipiency.

At least two-thirds of all patients with melanoma give a history of a pre-existing pigmented mole.[2] Over 50 per cent of this group state that this mole has been traumatized and in well over one-half of these cases a physician is responsible for the trauma. The usual story is that of coagulation of a nevus with an electrosurgical unit or a biopsy through the tumor or excision of a deeply pigmented mole with an insufficient margin. The careless injection of procain into the nevus or the passage of the hypodermic needle through the base of the mole may be sufficient to activate a quiescent pigmented tumor. A case has been reported in which a melanoma appeared shortly after a typhoid injection was given through a pigmented nevus.

The patient or circumstances may be responsible for the trauma under the following conditions:

1. Scratching or picking a mole.
2. Shaving over a nevus situated on the face or neck.
3. Rubbing the tumor with a towel or wash cloth.
4. Friction from constricting clothing as by a collar, hat band, belt or brassiere.

There are many kinds of nevi and the question arises as to which type is most prone to undergo malignant change. As a rule the deeper the pigmentation the greater the hazard. The most dangerous nevi have a shiny anthracite glitter or sheen. The more lightly pigmented are less dangerous but brown and even pink nevi have given rise to melanomas. The presence of hair in the mole makes malignant change less likely but does not rule it out altogether.

In view of all this, what steps should be taken to prevent melanomas from arising in pre-existing pigmented moles? Adair states that one school of thought advocates the excision of all pigmented moles. This is the counsel of perfection, desirable perhaps, but unobtainable. Pack, as the result of a detailed study, has determined that an adult has an average of 20 moles, which would make their excision impracticable. The other extreme is represented by those fatalists who advocate no treatment until the nevus shows evidence of malignant change.

A more rational middle ground would be followed if all deeply pigmented nevi and all moles, which by reason of their location, are subject to trauma, be excised as a prophylactic measure. Certain other nevi should be viewed with suspicion. Adair has pointed out the relative high incidence of malignant change in nevi situated about the feet and ankles. Fortunately nevi are less frequently on the lower than on the upper extremity. Moles which appear in the aged and any nevus which undergoes growth should be removed. Pigmented nevi on the genitalia or between the toes are especially hazardous. Negroes are less prone to melanomas than Caucasians but pigmented moles which occur on non-pigmented areas, as the sole of the foot or palm of the hand, should be excised promptly.

Pack[3] recently called attention to an endocrine factor in the relationship between pigmented tumors and melanomas. Despite definite clinical and microscopic evidence of malignancy in an occasional case in childhood, pigmented tumors which are excised prior to puberty do not recur, whereas similar tumors excised in adolescents just after the age of puberty show a higher recurrence rate than that encountered in older adults. This significant finding should lead to the excision of pigmented tumors which appear hazardous, whether by rea-

*Read before the annual meeting of the Medical Society of Virginia in Richmond, October 18-20, 1948.

son of their location or aspect, prior to the onset of puberty.

Certain precautions must be observed in the prophylactic excision of these tumors. The nevus must not be traumatized in any manner during the procedure. On theoretical grounds intravenous sodium pentothal should be the anesthetic of choice, but, if the patient demurs, a carefully administered local anesthetic probably carries a minimum of risk. The hypodermic needle must be inserted at a distance and the procain should be injected around and not into the immediate region of the tumor. The nevus must not be grasped by an instrument or manipulated in any manner. A sharp scalpel should be used and the nevus must not be coagulated. A margin of one centimeter should be given the tumor and the full thickness of the skin must be excised. A pathological examination should be made, for any tumor worth removing is worth examining microscopically.

If the nevus should also show deepening pigmentation or recent increased elevation, scaliness, bleeding or itching a much wider margin should be given than the one centimeter described above, for these changes should arouse suspicion of malignant change.

A certain number, fortunately small, will show unmistakable indications of malignancy when first seen. These are usually coal black, fungating or ulcerated tumors. Adjacent areas of stippling or actual daughter tumors about the primary lesion may be seen. If the tumor is growing very rapidly the metastases may not show the intensity of pigmentation which is present in the initial lesion. Enlargement of the regional lymphnodes indicates widespread involvement and a correspondingly poor outlook. An X-ray of the chest should be made to rule out blood borne metastases to the lungs.

If the lungs are uninvolved and the patient shows microscopic or unmistakable clinical evidence of a melanoma being present, a major excision is indicated. The primary tumor must be excised with a minimum of 6 to 10 cm. of adjacent skin. Skin grafting is frequently necessary. The underlying fat and fascia should be removed over an even greater area. If the regional lymphnodes are involved a block dissection of these glands should be made 10 or 14 days later. This interval of time is permitted to elapse in order to allow tumor cells, which may be migrating up the lymphatics at the time of the first operation, to reach the lymphnodes before these nodes are excised. If the lymphnodes are not involved clinically at the time of excision of the melanoma the block dissection of the regional nodes should be deferred until 5 or 6 weeks after the initial operation. Pack has been able to demonstrate metastases in 50 per cent of the lymphnodes which showed no gross evidence of involvement.

In recent years Pack[4] and his associates at the Memorial Hospital have been carrying out in suitable cases an "excision and dissection in continuity" for primary and metastatic melanomas of the skin. This procedure is based on the principles outlined by William S. Halsted in treating carcinoma of the breast. Halsted's operation entailed removal of the primary tumor, the adjacent skin, the lymphatics through which the tumor cells would pass and the lymphnodes into which these lymphatics drained, in one mass. By applying these same principles, Pack is able, in suitably situated melanomas, to remove widely the primary tumor as well as the lymphatics and lymphnodes with a large segment of skin, subcutaneous fat and underlying fascia.

If a melanoma arises on a finger or toe the accepted treatment has been to amputate the digit and follow this by a wide dissection of the axilla or groin. This, of course, does not obviate the danger of implants at any level in the extremity as a result of tumor cells lodging in the lymphatics.

In an effort to overcome this hazard, the Memorial Hospital group[5] have carried out more drastic procedures during the past few years. In cases where the primary lesion is situated too distant from the regional nodes to permit "excision and dissection in continuity", interscapulothoracic (shoulder-girdle) amputations have been performed for melanomas of the upper extremity. In the lower extremity melanomas of the foot with metastases to the femoral and inguinal glands have been treated by disarticulations of the hip-joint with retroperitoneal dissection of the iliac and obturator lymph nodes. Several hemipelvectomies (hind-quarter amputations) have been performed which entailed amputation of the lower extremity together with the innominate bone on the involved side. It may be found that a procedure of this magnitude is not only justified but indicated in what would otherwise be a lethal condition, but sufficient cases have not been followed over an adequate period to permit conclusions at the present time. The author

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feels that a procedure as mutilating and disabling as a shoulder-girdle amputation or hip disarticulation should be buttressed by an impressive five year cure rate before its general adoption is justified.

The question naturally arises as what results can be obtained by X-ray therapy in the treatment of melanomas. Many melanomas have been treated by radiation but the results have been uniformly discouraging. It is questionable whether a single five year cure has been obtained by this agent alone. Our only hope of effecting a cure at the present time is early and definitive surgery.

SUMMARY

1. Melanomas carry the highest mortality of any tumor arising upon the surface of the body.

2. Many apparently innocent pigmented tumors have rapidly metastasized following fulguration or other unwise forms of local treatment.

3. All pigmented moles which are subject to injury by reason of location and all deeply pigmented nevi should be carefully excised and examined microscopically.

4. Any evidence of activity on the part of a nevus, whether this be growth, itching, bleeding, ulceration, or increased pigmentation should be followed by an immediate excision with a wide margin. If the pathological report is positive for melanoma a definitive excision with subsequent block dissection of the related lymph nodes should be done.

5. The fate of the patient with an early melanoma rests in the hands of the first physician who sees him. Temporizing with such a condition or ill-advised methods of removal make the death of the patient inevitable.

REFERENCES

1. Pack, G. T., Perzik, S. L., and Scharuagel, I. M.: The Treatment of Malignant Melanoma. *California Med.* **66**:283, No. 5, (May) 1947.
2. Webster, J. W., Stevenson, T. W., and Stout, A. P.: The Surgical Treatment of Malignant Melanomas of the Skin. *Surg. Clinics of N. A.* (April), 1944.
3. Pack, G. T.: Prepubertal Melanoma of Skin. *Surg. Gynec. and Obst.* **86**:374, No. 3, (March) 1948.
4. Pack, G. T., Scharuagel, I. M., and Morfit, M.: The Principle of Excision and Dissection in Continuity for Primary and Metastatis Melanoma of the Skin. *Surgery* **17**:849, No. 6, (June) 1946.
5. Pack, G. T., Ehrlich, H. E., and Gentil, F. deC.: Radical Amputations of the Extremities in Treatment of Cancer. *Surg., Gynec. and Obst.* **84**:1105, (June) 1947.

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DISCUSSION

DR. ROBERT L. PAYNE, JR., Norfolk: It has been a pleasure to hear Dr. Warthen's paper. The subject has been covered in such a comprehensive fashion that very little remains to be said. It seems to me very important, however, that this subject should be brought to our attention from time to time. All too many of these tumors are still being wrongly or inadequately treated. It is the responsibility of the man who first sees a case of melanoma to be sure that proper treatment is carried out.

I should like to re-emphasize the point that Dr. Warthen has made about the prepubertal lesions. It is important to realize that although the local lesion removed in a child may have all the microscopic characteristics of a malignant lesion, it still will prove to be benign in its clinical behavior. For this reason radical surgery such as amputation and the wide lymph node dissections are not indicated. Pack states in a recent editorial on the subject that in over nine hundred cases of melanoma treated at the Memorial Hospital in New York there were no cases occurring prior to puberty in which metastases occurred.

It is important to remove suspicious lesions before puberty. It is important not to do extensive and unnecessary surgery before puberty.

There are two additional points which would indicate an endocrine factor in the development of these tumors. In pregnancy the occurrence of a melanoma has an extremely poor prognosis. Spread is usually very rapid and death occurs early. Patients who develop multiple skin lesions usually have an early death. However, there have been a few reports of marked improvement in this type of case following X-ray therapy to the pituitary gland. Wigby and Metz* report one case with complete retrogression of the skin lesions for as long as a year after treatment and this was as long as the patient had been followed at the time of their report. I wonder if Dr. Warthen can give us any more information about this type of treatment? I should like to make it clear that I agree that X-ray treatment of lesions or metastases is of no value.

Finally, I think a few words should be said about the occasional bizarre behavior of these tumors. While the average case with metastases survives for only a few years, a rare case will live for a remarkable length of time. There are reports in the literature of patients with known metastases who have lived for ten, fifteen or twenty years; one patient actually living for as long as twenty-five years.

We have in our records one patient with a somewhat unusual history. This man, aged fifty-five when first seen, had a melanoma removed from the right scapular region. Three years later a large mass of nodes were removed from the right axilla. Five years after the removal of the original lesion he developed an obstructing lesion of the cecum for which the customary resection

*Wigby & Metz: *Am. J. Roentg.*, 1939. **41**:415.

was done. All of these tumors proved to be identical histologically. Eight years after the removal of the original lesion he developed enlarged glands in the left supraclavicular region and died about one year after this, nine years after the removal of the original melanoma.

The fact that melanoma may spread either by the lymphatics or by the blood stream makes successful treatment difficult. Early involvement of the liver or lungs is common. However, since we cannot prevent the blood borne metastases, we can only strive to prevent lymphatic spread as outlined by Dr. Warthen.

I would like to thank Dr. Warthen for the opportunity of discussing his paper.

DR. WARTHEN, closing the discussion: I wish in turn to thank Dr. Payne for his courtesy in discussing my paper. He asked one question—if I had seen any cases of disseminated melanoma treated by radiation of the pituitary. So far as I know, a suitable case for this has not occurred in Richmond since this method has been suggested.

Women Doctors Faring Well.

Though still a medical minority, U.S. women physicians today occupy an important niche in the profession. Here are a few facts on their status garnered from a nationwide survey published in the June issue of *Medical Economics*, national business magazine for physicians:

Women practitioners net an average annual income of $7,929 (male doctors average $11,036). They devote nine hours a day to their medical practice (one hour less than men), spend an equivalent of 41 days a year in post-graduate study (eight days more than men). They allow 25 days a year for vacations (to men's 16 days). Only 12 per cent are in full specialty practice (as against 31 per cent of men).

New Books

The following are recent acquisitions to the Library of the Medical College of Virginia and are available to our readers under usual library rules:

Advances in surgery—vol. 1, 1949.
Barzilai—Atlas of ovarian tumors.
Bast—The temporal bone and the ear.
Bellak—Dementia praecox.
Brit. Med. Assoc.—The training of a doctor.
Burrow—The neuroses of man.
Cole—Operative surgery.
De Courcy—Pathology and surgery of thyroid tissue.
Fine—Care of the surgical patient.
Golden—For doctors only.
Gould—New Gould medical dictionary.
Gross—Surgical treatment of the abnormalities of the heart and great vessels.
Hermann—Clinical case taking.
Hess and Lundeen—The premature infant. 2nd ed.
Kopetsky—Deafness, tinnitus, and vertigo.
Kramer—Clinical orthoptics. Diagnosis and treatment.
Lawrence—The skin problem facing young men and women.
Meigs and Sturgis—Progress in gynecology.
Meleney—Treatment of surgical infections.
Menninger—Psychiatry in a troubled world.
Moodie—The doctor and the difficult child.
Mumey—Vaccination bicentenary of the birth of Edward Jenner.
Nielsen—Engrammes of psychiatry.
Pack—Cancer of the esophagus and gastric cardia.
Rusk—New hope for the handicapped.
Samuels—Nutrition and hormones.
Scheinker—Neurosurgical pathology.
Scobee—A child's eyes.
Thomson and Negus—Diseases of the nose and throat.
Tobin—Shearer's manual of human dissection.
Thorn—The diagnosis and treatment of adrenal insufficiency.
Trussel—Trichomonas vaginalis and trichomoniasis.
Van Ingen—The N. Y. academy of medicine. Its first hundred years.
Wespi—Early carcinoma of the uterine cervix.

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ACUTE PANCREATITIS*

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and
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We would like to present a review of the etiological factors and the present status of treatment in cases of acute hemorrhagic pancreatitis with particular emphasis on several phases which have been mentioned in the literature in the past but which we feel have not received sufficient notice. In addition, twenty new cases will be added to the literature, only three in detail, these being selected to illustrate one particular phase of acute pancreatic disease. The points which we wish to make in particular are: (1) The marked variation in the severity of the disease. In many cases there is only a mild edema with relatively mild symptoms and one is never worried about the outcome of the case. This mildness on one hand can be matched by an extremely catastrophic event which occurs suddenly and is marked by death within twenty-four hours in spite of intensive supportive therapy. Cases illustrating these two extremes will be presented. (2) A second point which we would like to stress is the finding of albuminuria which was present in a large percentage of our twenty cases. We have seen this mentioned in the literature only once.[8] (3) A third point which we wish to emphasize is that high blood amylase and lipase tests are a very great diagnostic help, but are not infallible evidence of acute pancreatitis. The most important factors in making the diagnosis are the history and physical findings. We have one case which is not included in the series but which is being presented showing an elevated blood amylase in a case of intestinal obstruction. In this case, operation was unduly delayed because of this laboratory finding. Had the blood amylase not been available, we feel that this patient would have received earlier and better surgical care. Polowe[12] has reported a case of high intestinal obstruction in which there was increased blood amylase activity.

Various authors have given definite names to the various stages of pancreatitis. Many feel that they are definite stages of the same disease while others feel that they are two or three distinct clinical entities. The most commonly used terminology is to divide these conditions into (1) acute edematous pancreatitis, (2) acute hemorrhagic pancreatitis, (3) acute pancreatic necrosis. It is our opinion that these are different phases of the same disease.

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ETIOLOGY

Lewison[7] in 1940 follows McWharter's classification which was published in 1932. In this classification acute pancreatitis is divided according to possible etiological factors. This is divided into main groups of infectious and non-infectious origin, and there is a third group consisting of a combination of two or more factors. In the non-infectious type, further subdivisions are: mechanical, chemical, traumatic or secondary degenerative changes in the pancreas. Morton's[9] classification, which was also published in 1940, adds to the possible causes mentioned above, alcohol, certain drugs, and circulatory stasis as possible causes for the disease. We feel in reviewing the literature that an occasional case of pancreatitis may well arise from such things as trauma, toxic conditions, and infection. However, certainly none of these can explain the vast majority of cases of acute pancreatitis. Archibald[1] stated in 1940 that "infection is practically always a late complication, the earlier lesions being found sterile." Eliminating the above possible rare causes of pancreatitis, we will discuss in more detail only a few of the more commonly accepted theories as to etiology.

1. Obstruction at the ampulla of Vater by a biliary calculus with reflux of bile into the pancreas was first brought out by Opie in 1901 and is probably the most commonly held theory at the present time. While a large percentage of cases of acute pancreatitis are associated with cholelithiasis or choledocholithiasis, there are certainly a large number in which no stones have been demonstrated either at operation, by x-ray, or at autopsy. Nevertheless, there are some strong points in favor of this

theory. In the first place, experimentally it has been found that if a stone is impacted in the very outlet of the ampulla of Vater and water is injected into the hepatic duct under pressure, a continuous channel between the biliary and pancreatic ducts with reflux of this fluid into the pancreas occurred in about 66% of the cadavers examined.[2] Reinhoff and Pickerell[15] found in examining two hundred and fifty apparently normal pancreases at autopsy that in about three-quarters of the cases the biliary and pancreatic ducts emptied together but that the common channel was shorter than the diameter of the duodenal orifice in all but 18%. Also it has been found that bile, if injected into the pancreatic tissue or back up the pancreatic ducts will cause a picture both grossly and microscopically similar to that seen in acute hemorrhagic pancreatitis.[1] A little added support to this common channel theory has been brought out by Popper[13] who demonstrated that pancreatic enzymes were present in the gallbladder in sixteen out of eighteen cases of acute pancreatic necrosis. Dragstedt[4] in 1931 found that the secretory pressure of the pancreas was greater than the secretory pressure of bile as determined by Mann and Giordano. Therefore, one would expect pancreatic enzymes to go into the biliary tract much more frequently than bile into the pancreatic ducts. Popper's theory is that this pancreatic enzyme is activated either while in the pancreas, in the common ampulla, or in the biliary passages following which there is a reflux of active trypsin into the pancreas.

2. Archibald feels that the cause of acute pancreatitis is frequently as mentioned above, but in addition there are many cases of acute pancreatitis which do occur and in which no common channel can be demonstrated between the biliary and pancreatic ducts or in which no stone is demonstrated in a duct with a common opening into the duodenum. In these cases he postulates the theory that the bile is brought into the pancreas by reflux up the pancreatic duct from the duodenum.

3. In 1936 Rich and Duff[14] came out with a new concept as to the etiology of acute pancreatitis. It is their belief that a large percentage of the cases can be best explained in the following way. There is a metaplasia of the epithelial lining of the small pancreatic ducts. This causes a damming up of pancreatic secretions behind the block with a resulting rupture of the acini. This allows trypsinogen to escape into the parenchyma of the pancreas. This trypsinogen is either already changed to active trypsin or is activated following escape into the tissues. This active trypsin erodes the walls of the blood vessels, causing the hemorrhage so frequently seen. In other cases where there is no hemorrhage, only the pancreatic tissue is damaged and no blood vessels are involved. This would correspond to the cases of acute pancreatic edema that one sees clinically and in which hemorrhage is not a large factor. In support of this theory, they found the same microscopic pathological picture of vascular necrosis in tissues of other parts of the body that were injected with trypsin. This picture was not present when the tissues were injected with bile. These findings are in conflict with those of Archibald[1] mentioned. Rich found metaplasia of the duct epithelieum with acinar dilatation in thirteen of his twenty-four cases of acute pancreatitis.

SIGNS AND SYMPTOMS

The usual signs and symptoms of severe acute pancreatitis are a sudden onset of pain in the mid epigastrium which rapidly becomes more severe and radiates both to the right and left and usually equally to both sides. By the time the patient is generally seen by the doctor, the pain is very severe and may radiate through to the mid upper lumbar region posteriorly. The other usual features are nausea, vomiting, abdominal distention, and frequently signs of shock. A subnormal temperature is not uncommon. Examination reveals marked tenderness throughout the abdomen, particularly in the epigastrium, with involuntary muscle spasm. The above is, of course, the picture of an acute pancreatic necrosis. In cases of pancreatic edema there may be no more symptoms than mild digestive upsets; and, as the pathology varies considerably, so do the symptoms which may be anywhere between these two extremes. There has been a case reported in the literature in which death occurred within twenty minutes of the onset of the first attack.[6]

DIAGNOSIS

In any patient with severe abdominal pain in the epigastrium, the diagnosis of acute pancreatitis must be considered. Of course, it is necessary first to eliminate other conditions which require immediate operation and which will be discussed in the differential diagnosis. When one questions the pa-

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tient, he should be sure to ask the location and duration of the pain and severity and to try to ascertain without leading questions whether the pain is present only in the anterior abdomen or whether it does go through to the back. If pancreatitis is suspected, a blood amylase or lipase estimation should be obtained. In chronic pancreatitis the blood amylase or lipase may be elevated for a long period of time while in the acute pancreatic necrosis these values are markedly elevated during the first twenty-four hours and then rapidly return to normal.[3] Sometimes they are relatively normal at first and then go up twelve or eighteen hours after the onset of the disease. Therefore, it has been suggested that these tests be performed every six hours in cases where the diagnosis is in doubt.

Another point which was demonstrated by Langerhans in 1890, but not often stressed, is the purely chemical cause of fat necrosis.[5] This is due to the escape of lipase from the damaged pancreas into the free peritoneal cavity with the neutral fat then being acted upon by the enzyme. The fats are split into glycerol and free fatty acids. The latter may be joined with calcium from the blood to form calcium soaps. This process in turn may cause a lowering of the blood calcium levels. For this reason, blood calcium determinations may be of value in the diagnosis of acute pancreatitis.[5] According to Edmundson, thirty-six of fifty clinical cases of pancreatic necrosis showed a serum calcium value below 9 mgm. per 100 c.c. of blood some time between the second and fifteenth day of the disease, but also Edmundson has studied a number of cases of perforated duodenal ulcer in which there was a moderate lowering of the serum calcium. For this and other reasons, blood calcium determinations, even when lowered, are not of great value in the differential diagnosis of this condition.

DIFFERENTIAL DIAGNOSIS

In considering the differential diagnosis, one is immediately struck by the many and varied conditions which may be confused with acute pancreatitis. This is only natural when one realizes the marked variation in symptomatology and severity of the pancreatitis itself. In the mild forms of pancreatitis, the diagnosis is frequently confused with peptic ulcer, gastritis, cholecystitis, and appendicitis. When the symptoms are mild, however, there is usually sufficient time and safety to obtain complete diagnostic workup, including x-ray examinations of organs which might be causing the difficulty. On the other hand, in severe cases of acute pancreatitis the conditions which are most easily confused are conditions which require immediate surgical operation. One of the most easily confused conditions is a perforated peptic ulcer. In both the onset is rather abrupt, although usually more rapid in the perforated ulcer. The pain of acute pancreatitis, while chiefly epigastric as stated, is usually more generalized than in the perforated ulcer where the pain and muscle spasm is usually confined to the epigastrium during the first few hours after perforation.

Acute cholecystitis as well as biliary colic due to impaction of gall stones in the cystic duct or passage of gall stones through the common bile duct is often most difficult to differentiate. In lesions of the biliary tract the pain is, however, most marked in the upper right quadrant with radiation to the right shoulder; whereas, in pancreatitis the symptoms are more in the epigastrium and periumbilical region with radiation to both sides equally and frequently to the midline of the back.

Many other conditions have been mistaken for acute pancreatitis. We have recently had a case of acute intestinal obstruction which was mis-diagnosed acute pancreatitis and for this reason operation was unnecessarily delayed. Because of this, we strongly urge that cases of acute pancreatitis be explored if the diagnosis is in doubt. We personally feel that acute intestinal obstruction is the abdominal disaster most easily confused with acute pancreatic necrosis.

Another condition which should be mentioned in the differential diagnosis is acute coronary thrombosis. From the Massachusetts General Hospital comes the report of a case so mis-diagnosed and reported in clinical pathological conference.[10]

TREATMENT

The primary treatment of acute pancreatitis is supportive. In the severe cases life can be maintained only with repeated whole blood transfusions. The use of whole blood is the one most important factor in the treatment, but this should certainly be supplemented with other intravenous fluids containing proteins, sugar, and salt. The water balance and blood chlorides should, of course, be main-

tained at the proper level. Severe distention is best combated with continuous gastrointestinal suction.[11] All other treatment is secondary to the above. It is, of course, necessary to give moderately large doses of narcotics for the relief of pain, and it is our feeling that the patients do better if they are not allowed to suffer unduly. Pain may be relieved by paravertebral blocks,[11] but we have had no experience with this. Whether operation is performed or not, all of the above measures should be carried out in the severest cases of pancreatitis. The decision as to whether to explore surgically or to treat the patient conservatively must be left entirely to clinical judgment, which is based on how sure is the diagnosis. It is our feeling that the patients are apt to do better if they are not operated upon, but to take any chance on allowing a perforated ulcer to remain open or not to relieve an acute intestinal obstruction is not warranted.

When operation is performed and acute pancreatitis found, it is generally our custom to place a drain into the lesser peritoneal cavity or into any pancreatic necrosis or abscess which might be present. If there are stones in the gallbladder, drainage of the gallbladder with removal of the stones is much simpler and probably safer in these severely ill patients than to perform a cholecystostomy at this time. If no stones are present, the question of biliary drainage is debatable. Dragstedt[4] believes biliary pressure should be reduced by cholecystectomy or choledochostomy. It is our feeling that this should be done if there is evidence of increased pressure, but is not wise if the gallbladder is not distended and no stones are felt in the biliary tract. Penicillin is generally given, but whether it is of any value in the treatment of this condition is open to question. Our feeling is that it should be given primarily to control any secondary infection which might arise. There is no pathological or physiological basis for believing that the penicillin *per se* is of any benefit in the treatment of pancreatitis itself.

After recovery from the attack of pancreatitis, every patient, we feel, should have x-rays of the gallbladder unless the exact condition prevailing within the gallbladder was determined at operation. If gall stones are present, an elective cholecystectomy should be performed a few months after the illness.

SUMMARY OF CASES

We have recently reviewed twenty cases of acute pancreatitis seen at the Jefferson Hospital. Of these twenty, the diagnosis was made at operation in seventeen. In two of the remaining three, the diagnosis was made at autopsy. In the twentieth case, no operation was performed and the patient recovered completely. We feel that this case, however, can be safely included in the series as the history and physical findings were rather typical of pancreatitis, and there was marked elevation of the blood amylase during the early stages of the disease with a later fall to normal. The sex instance is even, there being ten cases of each sex. In this series it was found that the disease is primarily one of young adult life, the ages varying from twenty-three to seventy, with fourteen out of the twenty being under the age of forty-five. In all but four cases, a history of chronic digestive complaints of some type was obtainable.

The duration of symptoms prior to operation varied from seven hours to six days. Both the white blood count and temperature were poor diagnostic signs. White blood counts on admission were obtained between the levels of 5,600 and 39,200. Mild leucocytosis was the usual finding. The degree of fever was even poorer in helping us to make the diagnosis or evaluate the prognosis. In six cases, admission temperature was subnormal. In two cases there was no urinalysis as the patients died before the admission urine was obtained. In sixteen out of the remaining eighteen case, albumin was present in the urine, being anywhere from a slight trace to four plus. This instance of albuminuria has been commented upon by Metheny, *et al.*,[8] but has not been generally stressed in the literature. In nine cases the gallbladder was definitely abnormal, whereas in four cases it was stated that the gallbladder was essentially negative at operation. In remaining cases, unreliable data was available.

The mortality rate is 35%, as seven out of the twenty died. Only three cases were not operated upon, and two of these died. However, the two who did die were not operated upon primarily because their condition was so poor at the time of admission that it was felt they could not withstand any type of operative procedure. Aside from this, to make any comparison of mortality rates in a series as small as this would be completely foolish.

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CASE REPORTS

1. The following case is presented as an example of a severe fulminating type of the disease: Mrs. D. R., age 70, was admitted to the Jefferson Hospital, September 21, 1947, with the complaint of lower abdominal pain, nausea, and vomiting. About one month prior to admission she had had a similar attack which was much milder and consisted of abdominal pain, nausea, vomiting, distention, and constipation. She was hospitalized for ten days elsewhere and gastrointestinal and gallbladder x-rays were essentially normal, while barium enema revealed only a diverticulum of the sigmoid. She slowly improved from this illness until two days before admission when the pain became much more severe, confined primarily to the lower abdomen on both sides and was associated with nausea and constipation. Examination on admission showed tenderness throughout the lower abdomen, most marked in the left lower quadrant. There was slight distention. There was no muscle spasm or rigidity and no masses could be felt. Temperature was 98°. General examination otherwise essentially negative. Patient did not appear acutely ill at this time nor during the night.

About twelve hours after admission the patient went into shock. The blood pressure could not be obtained, and the pulse was almost imperceptible within a matter of thirty minutes. Examination of the abdomen at this time revealed that it was more distended, very tense, and tender throughout. Her temperature was 100° by mouth. White count was 23,400. In spite of 1,000 c.c. of whole blood, 1,000 c.c. of plasma and saline solution, the patient's condition rapidly became more critical, and she expired about twelve hours after the sudden onset of her very acute symptoms. Postmortem examination revealed fat necrosis throughout the peritoneal cavity and a hemorrhagic type of necrosis involving the entire pancreas.

2. This case is presented to illustrate a milder phase of the disease and also one which was treated without operation: Mrs. N. D., age 25, was admitted to the Jefferson Hospital, October 14, 1947, with the complaint of abdominal pain. Present illness revealed that the patient had been awakened from her sleep with epigastric pain. The pain remained deep in her epigastrium and did not radiate and had been constant in character since it began. It was not relieved or made worse by the ingestion of food. There was nausea but no vomiting. Past history revealed no previous trouble with the gastrointestinal tract.

Physical examination: Patient was seen to be an obese young woman in moderate distress. She complained of epigastric pain. There was marked tenderness in the epigastrium and some voluntary muscle spasm, but no true involuntary spasm. No masses could be felt. Temperature on admission was 98.2° and white blood count was 5,600. The patient's general condition gradually became more severe during the next two days. White blood count two days after admission was elevated to 20,550 and the temperature had risen to 101.6°. The pain became more generalized throughout the upper abdomen, and there was some radiation to the back. Blood amylase was, therefore, obtained, and this was 87 mgm. %.* The following day with no treatment other than supportive therapy and penicillin 50,000 units q. 3 h., the white blood count had fallen to 12,000, and the patient's abdomen was not quite as tender as it had been. Blood amylase was 51 mgm. %. Two days later this had fallen to 14 mgm. %. Mild supportive therapy was continued. This included a transfusion as well as daily intravenous glucose. Her temperature remained elevated from 100° to 103° constantly for six days, following which there was a rapid return to normal during a period of forty-eight hours; and it remained normal during the remainder of her hospitalization.

3. This case is presented to show an example of pancreatitis which apparently was produced by trauma: Mr. R. S., 37 years old, was well until he was struck in his abdomen by a fist blow on July 8, 1947. He began having immediate cramp-like colicky, abdominal pain associated with nausea and vomiting. This was more severe the following day and then subsided. On July 10, 1947, he began to notice abdominal distention which was progressive up until his admission to the hospital on July 11, 1947. The discomfort in his abdomen had become more severe so that morphine had been necessary for the relief of pain the night before admission. Examination revealed an obese male in acute distress. The abdomen was markedly dis-

***Method of serum amylase determination used at Jefferson Hospital is the one proposed by Bray in his "Synopsis of Clinical Laboratory Methods." Normal values do not exceed 50. Values by the Somogyi method are roughly four times the values obtained by this method.**

tended and tympanitic. There was epigastric tenderness without any real muscle spasm. No peristaltic sounds could be heard on auscultation. Exploration was immediately performed, and it was found that there was severe fat necrosis. The pancreas was necrotic for an extensive region. Patient's condition was poor before operation, and he died twenty-four hours after operation. Autopsy revealed hemorrhage and necrosis throughout 90% of the pancreas with extensive fat necrosis of tissues within the peritoneal cavity. In view of the very definite history of trauma and the onset of pain at that time, it was felt that this is one of the cases which might fairly be classified as having trauma as an etiological agent.

4. A 30 year old woman entered the hospital on November 1, 1947, with the chief complaint of abdominal pain. For twelve days before her admission she had had severe recurrent sharp stabbing pains in her entire upper abdomen radiating straight through to both sides of the back. Pain also radiated into her lower back. Since the onset of her pain, she had had frequent bouts of nausea and occasional vomiting. The day before admission she vomited five times profusely. Past history is relevant in that she had an appendectomy and bilateral salpingectomy in July, 1947. Diagnosis at this time was pyosalpinx.

Physical examination on admission revealed a well developed and well nourished young woman in considerable distress, moaning and retching and complaining of stabbing pain in the upper abdomen and back. Examination of the abdomen revealed a low-grade tenderness in the upper abdomen; no masses, no definite spasm was noted. Otherwise the physical examination was essentially negative.

From the time of her admission on November 1 until early in the morning of the 4th, she did not actually vomit at all and received only mild sedation for her discomfort. On the morning of November 4, she began vomiting and had severe abdominal pain. Nausea and vomiting continued all through that day, and the abdominal pain was quite severe in spite of fairly large doses of narcotics. The abdomen at this time was essentially soft, and there were no definite high-pitched gurgling sounds. The morning of the 5th a blood amylase was obtained which was 71 mgm. %. She continued to vomit everything taken by mouth this day. Fluid requirements were maintained intravenously. Around midnight that night she suddenly went into shock, and large amounts of plasma and glucose were necessary to resuscitate her. She then began to vomit fecal vomitus. As soon as the patient was gotten into a little better shape, she was carried to the operating room and an emergency laparotomy performed. She was found to have enormously distended loops of bowel, but there was no evidence of gangrene. Adhesions were released and the abdomen closed as rapidly as possible. Her post-operative course was stormy, but at the time of her discharge on November 22, 1947, she was almost fully recuperated.

SUMMARY

1. A brief review of the etiology, diagnosis and treatment of acute pancreatitis has been given.

2. A summary of twenty new cases is presented with case reports of three of these.

3. Attention is called to the marked variation in severity of symptoms and also to the high incidence of albuminuria.

4. Elevated serum amylase may occur in high intestinal obstruction.

BIBLIOGRAPHY

1. Archibald, E.: Proceedings of The Institute of Medicine of Chicago, 1940, **13**:134.
2. Cameron, A. L., and Noble, J. F.: *Jour. A.M.A.*, 1924, **82**:1410.
3. Comfort, M. W.: *Minn. Med.*, 1941, **24**:225.
4. Dragstedt, L. R., Haymond, H. E., and Ellis, J. C.: *Archiv. Surg.*, 1934, **28**:232.
5. Edmundson, H. A., and Berne, C. J.: *Surg. Gyn. and Obstet.*, 1944, **79**:240.
6. Hatangdi, M.: *British Med. Jour.*, 1944, **2**:598.
7. Lewison, E. G.: *Archiv. Surg.*, 1940, **41**:1008.
8. Metheny, D., Roberts, E. W., and Stranalian, A.: *Surg., Gyn. and Obstet.*, 1944, **79**:504.
9. Morton, J. J.: *N. Y. State Jour. Med.*, 1940, **40**:255.
10. Castleman, B., and Parris, E. E.: *New Eng. Jour. Med.*, 1945, **233**:445.
11. Paxton, J. R., and Payne, J. H.: *Surg., Gyn. and Obstet.*, 1948, **82**:69.
12. Polowe, D.: *Surg., Gyn. and Obstet.*, 1946, **82**:115.
13. Popper, H. G.: *Amer. Jour. Diges. Dis.*, 1942, **9**:186.
14. Rich, A. R., and Duff, G. L.: *Johns Hopkins Hosp. Bull.*, 1936, **58**:212.
15. Reinhoff, W. F., Jr., and Pickrell, K. L.: *Archiv. Surg.*, 1945, **51**:205.

DISCUSSION

DR. R. P. BELL, Staunton: Mr. President and Gentlemen: Dr. Trout's paper brings up a subject about which there has been quite a lot of new study and new thought,

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and, of course, such papers are always timely and valuable; that is, when they are properly prepared and properly presented, as is his.

The pancreas, as we all know, is an organ about which all too little is known, although we must admit that a great deal has been found out concerning it during the last five or six decades. We have known, of course, for a long time about the digestive ferments that are originated in the pancreas—amylopsin, steapsin, trypsin, and rennin. The discovery of insulin,—that spectacular occurrence—brought out the fact that this internal secretion of the islands of Langerhans has absolute control over sugar metabolism. We have found out in recent years, from a surgical standpoint, that the whole pancreatic organ can be removed and the patient live by administration of the enzymes and insulin. The monumental work of Whipple, Mulholland and others along this line has been mentioned. But we are brought face to face frequently, to our chagrin, with the fact that of the inflammations of the pancreas we are still woefully ignorant.

I think the first operations for pancreatitis were done back as far as 1883. From that time up to about 1930 acute pancreatitis was thought to be a very virulent, rapidly fatal disease never diagnosed until operation was done for something else. Along about 1930 we began to have a new thought on the subject of pancreatitis and began to realize that it is not primarily an infection but is a chemical change brought on by the stoppage of the ducts and rupture of the capsule, with a pouring out of the enzymes into the abdomen. Therefore, the point was brought out, why operate when we can make the diagnosis? But the sad part is that we often cannot make it. Take the series of cases Dr. Trout has presented. Out of twenty cases, seventeen were diagnosed at operation and two, I believe, at autopsy. I have seen several other series presented in which about the same percentage of preoperative diagnosis was made.

As to the causes, our thought is pretty well crystallized that there is a damming up of the pancreatic fluids, either by a stone or other obstruction, causing bile to dam up in the pancreatic ducts, causing rupture of the acini and allowing trypsinogen to escape into the parenchyma of the pancreas.

The symptoms, of course, we know pretty well. This condition is frequently confused with other things—appendicitis, peptic ulcer, gall bladder disease. Sometimes coronary disease may confuse us.

As to treatment, I think our thought is pretty well crystallized that we should not operate on these patients. The difficulty is to know when we have a pancreatitis. Since 1930, when most of the cases died, the statistics have been very much better.

What are we going to do about it? Is this a surgical or is it a medical problem? I think it is a medical problem, but I notice that the surgeons are writing all the papers. When a medical man gets a patient with high abdominal pain, tenderness, and so forth, he usually calls in a surgeon, and I think it is right and proper he should do so. I think the medical men and the surgeons should work together on these cases in order to reach the proper diagnosis.

The history, of course, is the important thing. The amylase test is a great help, and I think all hospitals should be equipped to do it. Every hospital ought to have a laboratory technician trained to do these tests and do them accurately, and I think there are a great many hospitals that are not so fixed. The points to be stressed are careful examination, the use of this test, and, when in doubt, operate. With the anesthetics that we have these days a simple opening of the abdominal cavity is scarcely a hardship on any patient; and it is very much better to operate, because there may be ruptured peptic ulcer, than to wait too long watching the patient because you think it is acute pancreatitis.

DR. J. MORRISON HUTCHESON, Richmond: I wish to commend Dr. Trout for his excellent paper on this important subject. Acute pancreatitis is probably far more common than we realize. Dr. Trout has touched upon the variableness of the picture. It seems likely that while the more severe cases manifest symptoms and signs that permit recognition, there are milder cases that escape detection because the symptoms are slight or because we fail to think of this condition.

The diagnosis of acute pancreatitis is largely a clinical one. The presence of increased serum amylase is undoubtedly important but the elevation is transient and may easily be missed, and its absence should not argue too strongly against pancreatitis. Serum amylase may also be increased in other conditions. One of the highest levels I have seen occurred in a patient with a ruptured gall bladder.

DR. TROUT, closing the discussion: I should like to thank Dr. Bell and Dr. Hutcheson for their remarks.

With reference to Dr. Bell's remark as to whether acute pancreatitis should be treated by a medical man or by a surgeon, I certainly agree with him that there should be close cooperation between the two. While it is a medical condition it seems hard to believe that a medical man can treat the great majority of these patients alone, because so often acute abdominal catastrophe which requires immediate surgical intervention must be considered; and I think the surgeon should be called in.

I would like to stress particularly Dr. Hutcheson's remarks. I agree with him that the presence of increased serum amylase is of great help, but its absence does not rule out pancreatic disease. The elevation is extremely transitory. In some cases it may rise in the first twenty-four hours and then fall to normal. In chronic pancreatitis it may be slightly elevated over a long period of time. It has therefore been suggested that in these cases the blood-amylase test be repeated every six hours for the first two or three days. If this is done, an elevated serum amylase may be found on a later examination which would be missed if only one determination were made.

AN UNUSUAL CASE OF HYDROCEPHALUS WITH SOME COMMENTS ON DELIVERY

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Newport News, Virginia.

A 34-year old multipara was found to have a breech presentation about six weeks before the expected date of delivery. An X-ray taken to confirm the clinical impression revealed a huge hydrocephalus in the frank breech position. The hydrocephalus had not been suspected. As term drew near the size of the abdomen increased markedly especially in the upper portion. The enlarged fetal head finally could be palpated most easily. The patient went into spontaneous labor at the 41st week. For a long time the uterine contractions were irregular and not very strong. After 18 hours the cervix had dilated only 4 cm. At this point the membranes were ruptured in the hope that the release of intrauterine pressure would improve the quality of the labor. Following this the strength of the uterine contractions was indeed increased and in several hours the cervix was completely dilated.

Study of this case beforehand had convinced me that the head was too large to engage in the pelvis. And so it was. The buttocks delivered spontaneously, the legs were brought down and about two-thirds of the body was easily delivered. Here the delivery came to a standstill. Further progress was impossible because the head was arrested at the pelvic inlet; it was up in the abdominal cavity out of reach for perforation through the vagina. Anticipating this difficulty, I had come to the delivery room armed with a long metal cannula which I planned to insert up the spinal canal after cutting down on the most accessible portion of the vertebral column. But it so happened that the fetus had a spina bifida along its entire lumbar spine. The cannula was therefore inserted into the spinal canal through this ready-made opening and easily passed up into the cranial cavity (figure 1). Cerebrospinal fluid spurted out through the cannula and in a few minutes the head was so reduced in size it entered the pelvis. The remainder of the body then delivered and the head itself was easily brought forth by grasping the infant by its ankles and swinging its body back on the mother's abdomen. Even in the collapsed state the head circumference (occipito-frontal) was 45 cm., or 10 cm. more than that of a normal newborn. The baby weighed 8 lbs. 2 oz. (3685 gm.). The fetal heart was heard when the mother was brought to the delivery room, but the infant was stillborn. Death was attributed to the delay in the delivery of the head. Due to an oversight no autopsy was obtained.

Delivery of the hydrocephalic infant presenting by the breech is usually handled without difficulty by perforating the after-coming head following delivery of the body. In the case just reported the problem was more difficult in that the head was too large to engage in the pelvis. The head remained in

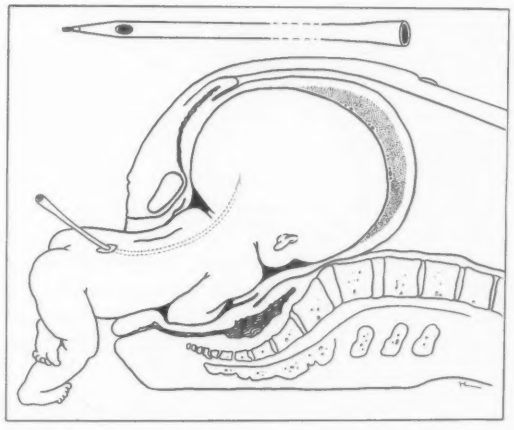

Fig. 1

the abdominal cavity out of reach through the vagina. This impasse was overcome by passing a cannula up the spinal canal to the cranial cavity. Mother Nature made the task easier by providing a spina bifida so that it was not necessary to cut down on the vertebral column. To enter the spinal canal, an incision is made in the midline over the spinous processes. The skin edges are retracted by Allis forceps, the laminae are incised with the scalpel and the fragments removed. A semi-rigid waxed silk urethral catheter* is then passed through the defect in the vertebral arches on up to the cranial cavity. If such a catheter is not available

*Catheters are ideal for this procedure in that they are always to hand. In my own case I happened to have a long metal cannula which was almost straight.

one can use an ordinary soft rubber catheter into which has been inserted a length of stiff wire. Insert the wire into the catheter just short of the eye, for if it protrudes through the eye it may get snagged in the spinal canal. Bend the far end of the wire to a right angle or more so that it does not advance further into the catheter.

Where the after-coming head is engaged in the pelvis and the entire body has been delivered, the method of Gustafson is very satisfactory (figure 2).

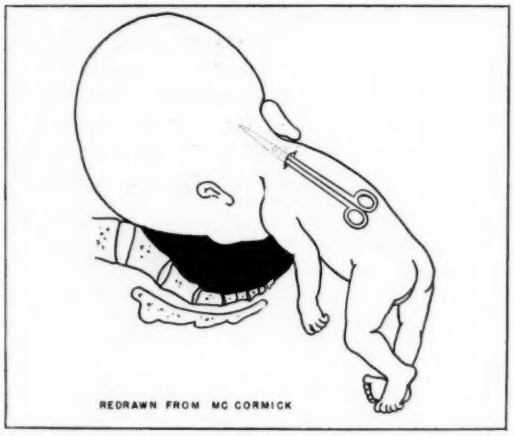

Fig. 2

A transverse incision is made in the skin at the base of the neck and then the scissors or the perforator are tunneled beneath the skin to the base of the occiput, thus protecting the maternal soft parts from injury.

In breech hydrocephalus the practitioner has at least a purchase hold on the fetus through its body, which, being smaller than the head, will be expelled in whole or in part. When the hydrocephalus presents by the vertex the problem is obviously different. It constitutes one of the most dramatic examples of cephalopelvic disproportion. The use of cesarean section for this type of case has been roundly and repeatedly condemned. Yet the treatments which have been recommended for so many years, such as craniotomy, perforation and version, etc., are more dangerous than cesarean section. Therefore, some practitioners turn to cesarean section in order to insure the survival of the mother.

All of the classic technics for delivery of the vertex hydrocephalus insist on complete dilation of the cervix as a preliminary. However, full dilatation occurs slowly in hydrocephalus, the labor often being very inefficient and prolonged. The length of labor required for full dilatation can seriously overstretch an already markedly distended lower uterine segment. Version and extraction run the risk of rupture of the uterus because of the thinning out of the lower segment. Craniotomy runs the risk of deep laceration of the birth canal by fragments of the crushed skull.

O'Connor and Gorman[1] solved this dilemma of treatment in a most simple manner. Early in labor when the cervix was only a few centimeters dilated they inserted a spinal needle into the head of the fetus and drew off enough fluid to reduce the size of the head. The results were excellent. The patient was a primipara with a vertex hydrocephalus. The cervix was 3 cm. dilated. These authors ruptured the membranes and inserted a No. 18 spinal puncture needle into the head (figure 3). Cerebrospinal fluid spurted out and whenever the stream slowed it was accelerated by pressure on the head through the abdomen. About 1400 cc. of fluid were removed. Adequate uterine contractions set in almost at once and in just one hour the infant was delivered spontaneously. It died two hours after birth.

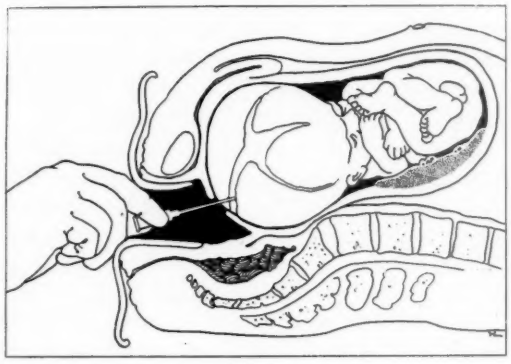

Fig. 3

O'Connor and Gorman called their procedure intraventricular tap and drainage. It has many advantages. One does not wait for complete dilatation of the cervix. All that is required is enough dilatation to permit insertion of the needle into the fetal head. Prolonged labor is avoided. The dangers of a long labor are not added to the dangers of an already over-stretched lower uterine segment. Intraventricular tap and drainage may be done by the general practitioner. Special skill and training are

not required as in craniotomy, perforation and version, etc. No anesthesia is needed for intraventricular tap and drainage. After the head has been drained of excess fluid it engages in the pelvis and can be delivered in due course either spontaneously or by low forceps.

Intraventricular tap and drainage of the hydrocephalic head is a safe, simple means of obtaining easy delivery through the vagina. Perforation of the vertex is an easy matter. The skull bones are thin and the fontanels are widely open. The distention of the ventricles of the brain is so great that the brain tissue over the vertex is compressed into a thin layer. The essential point about intraventricular tap and drainage is that the spinal needle is inserted into the fetal head in early labor as soon as there is enough dilatation to insert a spinal needle through the cervical canal. *One does not wait for complete dilatation of the cervix.* Here is the overwhelming superiority of the method over the classic technics. Intraventricular tap and drainage avoid the risks of prolonged labor, rupture of the uterus, pressure necrosis, fistulas, postpartum hemorrhage from atony of an over-distended uterus or lacerations of the birth canal.

There may be a rare case of vertex hydrocephalus where the cervix is difficult to expose or the head cannot be brought within reach of the needle through the vagina. Here intraventricular tap and drainage may be done *through the abdominal wall,* after the method of Walsh,[2] of Liverpool. The bladder is emptied by catheter. The skin of the abdominal wall and the peritoneum is anesthetized with 1 per cent novocaine in the midline over the head (usually this site is midway between the symphysis and umbilicus). A No. 16 spinal needle is then passed through the abdominal wall, uterus and head into the ventricles. Very little effort is needed. The procedure is quite painless to the mother and there is no need to try to pass the needle through a fontanelle or suture. The needle passes readily through the deficiently ossified skull. A 20- or 50-cc. syringe is then fitted to the needle and the cerebrospinal fluid aspirated after which the needle is withdrawn.

The four simple technics reviewed in this paper make possible safe, simple, easy delivery through the vagina for the hydrocephalic case whether it presents by the breech or vertex, whether the body is completely or only partially delivered, whether the head is high or low. Plass[3] pointed out recently that these procedures have greatly simplified the management of hydrocephalic labors although they are rarely mentioned in standard textbooks. "They are so much simpler than the classic technics that their general adoption would seem indicated." It should be stated that the most recent editions of McCormick, De Lee-Greenhill, and Mengert mention or describe some or all of these simplified technics. Generally speaking, vaginal delivery is 10 times safer than cesarean section. Therefore, the vaginal route is to be preferred for the delivery of hydrocephalus now that the safety of this route is assured. There is no need to have recourse to the dangerous and complicated technics of craniotomy, perforation and version, etc. By the same token, "cesarean section with its attendant maternal risk, performed for a child who is virtually biologic waste, is a completely irrational method of therapy for hydrocephalus" (Mengert[4]).

Are there any religious objections to the technics which have been recommended in this paper? It is well to consider this aspect of the subject because there are millions of Catholics, hundreds of Catholic hospitals, and thousands of Catholic doctors in this country. The Catholic Church forbids craniotomy as long as the infant is alive. This is because craniotomy involves destruction and evacuation of the cerebral contents. Any cranial operation is forbidden which has for its purpose the direct killing of the fetus.[5] However, tapping the fetal head with a trocar and cannula has been approved by Catholic moralists, says McCormick.[6] "The procedure is not necessarily synonymous with fetal death, and cannot be described as an attack on the fetus any more than a cerebral operation on an adult is an attack on him. It is done for the sake of both the child and the mother; to save the mother from death from a ruptured uterus, to give the child the only thin chance of life and Baptism, which is possible for him aside from having recourse to cesarean section . . . Although cesarean section in handling a case of dystocic hydrocephalus is allowed, ecclesiastical opinion does not require it peremptorily." And Walsh,[2] whose procedure has been described above, says, "I am advised on the highest ecclesiastical authority that there is no objection on religious grounds (to tapping the hydrocephalic head with a spinal needle). The aim of the treatment is to reduce the size of the head to

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make spontaneous labor possible and to prevent obstructed labor."

It must be remembered that tapping or mere perforation of the greatly dilated and thinned out brain does not as a rule cause fetal death.

A Catholic point of view attributed to Moore is quoted by O'Connor and Gorman,[1] "The operation of craniotomy involves two stages: (a) perforation of the skull; (b) complete destruction of the cerebral contents . . . If the second stage of the operation is omitted and the physician attempts to effect delivery with as little loss of cerebral substance as possible and does all he can to save the life of the child he is no longer making a direct attempt to kill the child but in certain rare instances in which delivery may be otherwise impossible, he will be doing all he possibly can do to save the lives both of the child and of the mother."

In the case of breech hydrocephalus, the body will be born first and this will allow the performance of baptism. The infant will almost inevitably succumb to the delay in delivery of the greatly enlarged head. One then proceeds to reduce the size of the head by tapping and draining off the excess fluid. This can be done either by passing a scissors up under the skin of the neck to the base of the occiput or by passing a catheter up the spinal canal, depending upon the accessibility of the head. Churning or stirring up the cerebral contents with the scissors or other instrument must be strictly avoided, for in case there is still a spark of life in the infant it would be destroyed. This action would violate Catholic moral concepts.

O'Connor and Gorman[1] approached the problem of delivery of the vertex hydrocephalus from a Catholic point of view. They were concerned with delivering the infant alive by some means other than cesarean section. In the method of intraventricular tap and drainage they found a means which not only met their theological requirements but which is overwhelmingly superior to the classic technics as regards ease, safety and rationality. The need for both craniotomy and cesarean section in the treatment of hydrocephalus no longer exists. Cesarean section can be justified only if there is an associated complication which requires the operation *per se* such as placenta previa.

SUMMARY

1. A case of breech hydrocephalus is reported where the head was too large to engage in the pelvis and only a portion of the infant's body could be delivered. Delivery was effected by draining the head through the spinal canal.

2. Consideration is given to the management of hydrocephalic births in general. The older technics are evaluated in the light of recent advances and found wanting.

3. Four simple, improved technics are recommended which permit safe, easy delivery of the hydrocephalus through the vagina regardless of presentation.

4. These simplified technics are shown to be permissible with Catholic patients because they do not directly attack the life of the fetus. They can therefore be used universally whatever the religious affiliation of the patient, the physician or the hospital. This makes it possible to standardize the management of the hydrocephalic labor case.

5. It is urged that craniotomy, perforation and version, and other classic technics for the delivery of hydrocephalus be abandoned because they require full dilatation of the cervix, prolonged labor, and dangerous complicated manipulations in an overdistended uterus.

6. It is urged that cesarean section be abandoned because with these simplified technics there is no longer any justification for subjecting a woman to abdominal operation for the sake of a monster.

BIBLIOGRAPHY

1. O'Connor, C. T., and Gorman, A. J.: The Treatment of Hydrocephalus in Cephalic Presentation, *Am. J. Obst. and Gynec.* **43**:521, 1942.
2. Walsh, C. H.: Foetal Hydrocephalus, *The Medical Press and Circular* **201**:380 (April 19), 1939.
3. Plass, E. D.: Drainage of a Hydrocephalic Head, *Am. J. Obst. and Gynec.* **56**:548 (March), 1948.
4. Mengert, W. F.: Postgraduate Obstetrics, New York, Paul B. Hoeber, Inc., 1947, p. 266.
5. Maher, R. A.: Catholic Moral Medical Code, Toledo, Diocese of Toledo, 1948, p. 11.
6. McCormick, C. O.: Pathology of Labor, the Puerperium and the Newborn, St. Louis, C. V. Mosby, 1947, p. 487.

2914 West Avenue.

A METHOD OF TREATMENT OF MASSIVE GASTRO-INTESTINAL HEMORRHAGE WHICH APPEARS UNCONTROLLABLE*

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One of the difficult types of gastric hemorrhage to handle is that in a patient more than 50 years of age, where a sclerotic vessel along the wall of the stomach or in an adjacent structure has become eroded by an ulcer. The vessel at autopsy is seen to be wide open and surrounded with the dense scar tissue of the ulcer. Probably no procedure we may follow would completely solve the surgeon's problem in all these cases. Two case histories are given, illustrating how two such cases were handled successfully.

W. H., a 52 year old white veteran, was admitted February 28, 1948, for gall bladder disease. He had an attack of abdominal pain six months previously. Roentograms made revealed what was thought to be a duodenal ulcer.

His present attack of pain began ten days prior to admission. He was nauseated at times, but did not vomit. Food did not relieve the pain. He also had pain in the right kidney region and complained of hematuria. The ward surgeon proceeded to work him up from the genito-urinary angle. Early in the morning of March 10, 1948, he became nauseated and started for the bathroom when he "blacked out." The ward nurse found him on his hands and knees in a pool of bright red and clotted blood which he had vomited. When he was placed in bed, his blood pressure was found to be 80/40, when it was ordinarily 130/90. His hemoglobin dropped from 14.5 on admission to 8.5 that morning. He was given plasma while a donor was obtained. He was given nothing by mouth for twelve hours, then was put on a Muelengracht diet. He was given a mixture of milk with alkalies hourly. He was also given transfusions on the two succeeding days. Stools were tarry, but there was no more evidence of copious hemorrhage until March 13, 1948.

In this second episode of profuse hemorrhage, his hemoglobin dropped to four grams, with 1,500,000 red cells, and his pulse, which could not always be counted, rose to 140. He was given 2,500 c.c. of blood during the next 24 hours and a surgical consultation was requested.

Since the patient was in extremely poor physical condition for emergency surgery, the following procedure was adopted to make a diagnosis and to get the patient in a better physical condition for any indicated surgery: (1) Bed rest; (2) Constant nursing care; (3) Gastric evacuation continuously, using a #18 French gastro-duodenal tube; (4) Frequent lavage of stomach by encouraging patient to drink ice water; (5) Reduction of gastric acidity by irrigating the stomach through the gastro-duodenal tube hourly with 30 c.c. of soda bicarbonate solution, ounces one to eight ounces of water. The patient was given demerol for pain, vitamin K, protein hydrolysates, electrolytes, fluids to meet the body needs, and the use of tobacco was interdicted. His blood pressure, electrolytic balance, and blood protein were checked frequently.

The return from the stomach was bloody at first. This, however, cleared in four or five hours. The gastro-duodenal tube was removed after four days. There was no recurrence of bleeding. After the tube was removed, he was given not more than one ounce of water every hour. He was also given amphogel, drams one hourly, during the day, and atropine, grains 1/100, hypodermically every 4 hours. The second day he was given milk ounces one every hour. This was increased as he tolerated it better. His blood count and hemoglobin were brought to former levels with repeated blood transfusions. A roentogram March 21st revealed a duodenal ulcer with a crater. A gastric resection was done April 7, 1948. An ulcer which had perforated the first portion of the duodenum into the pancreas was found. The floor of the ulcer in the pancreas was covered with thin granulations through which a large vessel was visible. This vessel, no doubt, had been eroded and the hemorrhage issued from the erosion. The patient received 7,000 c.c. of blood during his hospital stay. His recovery was uneventful and he returned to his work as an electrician.

*Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

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The other case was that of a 65 year old, retired soldier, admitted April 6, 1948, with a history suggestive of gastric ulcer for twenty years. The admitting physician also thought of the possibility of cirrhosis of the liver. He was transferred to us from an Army Hospital, where he was treated six days and given a tentative diagnosis of carcinoma of the stomach. While there he was digitalized because of evidence of cardiac failure. During those six days he had a severe hemorrhage, with hematemesis. His blood pressure dropped to 70/40, and his hemoglobin from 11.5 to 6 grams. While in the Army Hospital, he was given three transfusions of 500 c.c. of blood each. When he was transferred to the Veterans Hospital, he was given a transfusion because of anemia. The following day his red cells were 1,800,000, and hemoglobin 5.5 grams. He did not show improvement after two more transfusions and was turned over to the surgical service. Since the patient's condition was very poor, the same regime was used on him as on patient number one, except that an attempt was made to save the services of a special nurse. He was placed in a ward with another patient who required constant care, and these two patients shared one attendant. This proved to be a mistake. The patient pulled out his gastro-duodenal tube three times in the first 48 hours, and at the end of that time had a minor hemorrhage. He was then given a special nurse. The return from his stomach cleared up in a few hours and he had no more bleeding. Gastric evacuation was discontinued after five days. A gastro-intestinal roentogram April 19, 1948, revealed what was thought to be a duodenal ulcer. The patient had a gastric resection April 30, 1948. An ulcer of the stomach with perforation into the pancreas was found. The ulcer was near the lesser curvature posteriorly. The pathologist reported two points of projecting eroded vessels occluded by an organizing thrombus in the ulcer. The patient had an uneventful recovery and returned to his home in retirement.

This method of treatment has been used on other patients with hemorrhage from ulcer, with equal success. The two cases are presented because they illustrate hemorrhage from ulcer that is difficult to control. It is believed that points in favor of this method of treatment are: (1) The stomach is put at physiologic rest; (2) Acidity of the stomach is controlled; (3) The surgeon is warned promptly if hemorrhage recurs; (4) The hemorrhage is checked temporarily, giving time to make a diagnosis by roentogram, and to build the patient up for operation.

SKF Laboratories Awarded Grant for Cancer Research.

One of the first grants for cancer research from the National Cancer Institute to a non-academic research center has been awarded to Smith, Kline & French Laboratories, Philadelphia pharmaceutical manufacturers. The grant, in the amount of $10,800, will be administered by Dr. Glenn E. Ullyot, head of the organic chemistry section of the firm's research laboratories.

Dr. Ullyot's investigations will center around colchicine, an alkaloid derived from the bulbous herb known as meadow saffron or autumn crocus. This substance is known to arrest multiplication of cancer cells in experimental animals, but it is also injurious to the normal cells. Preliminary research with closely related compounds indicate that there may be some hope of developing colchicine derivatives with a more specific action against the disease. Already widely experienced in colchicine chemistry, Dr. Ullyot will extend his studies in an attempt to find a cancer-inhibiting compound that will not damage the host.

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PUBLIC HEALTH

L. J. ROPER, M.D.,
State Health Commissioner of Virginia.

The report of the Bureau of Communicable Disease Control of the State Department of Health for August 1949 as compared with the same month in 1948, and for the period of January through August 1949 compared with the same period in 1948, is as follows:

	Aug. 1949	Aug. 1948	Jan.-Aug. 1949	Jan.-Aug. 1948
Typhoid and paratyphoid	21	13	91	93
Diarrhea and Dysentery	1,402	614	3,914	2,770
Measles	136	97	21,237	6,063
Scarlet fever	24	16	456	611
Diphtheria	9	10	92	143
Poliomyelitis	109	152	161	258
Meningitis	11	7	66	67
Undulant fever	4	3	42	60
Rocky Mountain spotted fever	27	19	86	58
Tularemia	6	5	25	41

RESULTS OF ANTIBIOTIC THERAPY

There is a growing and gratifying tendency upon the part of physicians, in reporting certain types of communicable diseases, to report upon the results of antibiotic therapy. We heartily appreciate these treatment reports and hope the physicians will continue to send them. Though not primarily responsible for treatment, this being the function of the private physician, the State Health Department would like to act as a clearing-house of practical information in regard to treatment results. Since we send out weekly morbidity reports to all reporting physicians of the State, these weekly reports may well serve as a two-way channel of information of communicable disease incidence and results of treatment.

In reviewing these treatment notes on reports of communicable diseases of the last few months, we find reference to the successful use of antibiotics in Rocky Mountain spotted fever, typhoid fever, undulant fever and atypical pneumonia. The most dramatic of these clinical reports have concerned the treatment of Rocky Mountain spotted fever with Aureomycin. In cases reported, fever, prostration and rash have responded within 48 hours to intensive Aureomycin therapy. One report showed similar prompt results with the use of Chloromycetin. In line with the results obtained by other clinicians the reports from our physicians show equally excellent results from the use of Aureomycin in acute brucellosis. These reports are most encouraging when we recall the unsatisfactory treatment of undulant fever before the advent of the antibiotics.

On the laboratory side, the limited experience of our State Health Department Laboratory in the examination of blood specimens from Rocky Mountain spotted fever cases treated with antibiotics for complement-fixing bodies and non specific agglutinins, as demonstrated by the Weil-Felix reaction, indicates that there is an increase in titre as shown by both tests in spite of antibiotic therapy. However, the increase in titre does not attain the levels found in these cases prior to the introduction of this therapy.

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MEDICAL SOCIETY OF VIRGINIA
PUBLIC RELATIONS

HENRY S. JOHNSON, *Director*

Reception Room and Literature.

It seems that compulsory health insurance will not be inacted in 1949. The President's Reorganization Plan No. 1 also seems dead, although the philosophy, politics, and the pressure of both of these should not be ignored.

Of course, we can expect proponents of government medicine and the extension of other government services, to be very active during 1950 under the leadership of a President sharing their point of view.

Dentists and Pharmacists in Virginia are cooperating nicely in our educational campaign. They are helping in speaking engagements, in discussion groups, with the distribution of literature, talking with influential people, and in getting resolutions to Washington.

It is hoped that every member of the Medical Society of Virginia will (beginning not later than October 1), make conspicuous display of the Fildes painting of "The Doctor" and of literature pertinent to the subject of compulsory health insurance.

Ample literature is in the office, but orders are not coming in. It will take individual and combined effort to carry this story to the people. You are urged to join in now.

Prepayment Plans Said to be Exploited.*

Dr. H. Boyd Stewart, President of the American Society of Anesthesiologists, recently stated: "From many sources over the United States, I am hearing increasingly numerous reports that surgeons and anesthesiologists are being cited in contempt by the public in their relations with patients who are insured under Blue Cross and Blue Shield Plans."

He went on to say that "the universal charge against the physician is that he is guilty of exploitation of his patients by accepting a fee from a pre-payment plan and then charging the patient a private fee as large as he was accustomed to levy before the patient had insurance."

He indicated that patients are asking the question, "Who is the one insured and protected under these voluntary plans, the patient or the physician?"

Dr. Stewart indicated that "most of these voluntary plans had been sponsored by, and are being operated under the supervision of the medical profession, and that the success of it depends almost entirely upon the integrity and cooperation of the profession."

He stated further, in part, "It behooves the individual physician who participates and who is reimbursed by these plans to use discretion and observe honesty, lest he inadvertently contribute to a justifiable wave of resentment."

(*Taken from the "President's Page" of the Newsletter of the American Society of Anesthesiologists, Inc., August 1949.)

Editor Looks at British Medicine.

After five weeks in Great Britain and a study of their system of socialized medicine, John W. McPherrin, editor of *American Druggist,* stated: "It is our conclusion that there is no hope, peace of mind, or real security for anyone in the belief that 'The State is my Shepherd, I shall not want.' This is the real concept of the welfare state and—nothing, not even a free health service is more important to a nation that the spirit of its people."

He adds that "so far as the British Health scheme is concerned, it is a major expression of the welfare state idea, and as a health scheme, it is very similar to the plan President Truman has proposed for this nation."

Mr. McPherrin continues, "If this nation of ours should ever adopt the same kind of a scheme, we must be prepared to accept the same increase in taxes and government controls. . . ."

It is believed that "security" would not be found in the "socialist idea" that "the state is my shepherd", for acceptance of this idea could lead to a deterioration of the medical services, and a loss of faith in the individual.

Thanks to Our Senators!

The U. S. Senate on August 16th rejected by a vote of 60 to 32 the President's reorganization Plan

No. 1, which would have created a Department of Public Welfare under which Federal medical services would have been included. Senator A. Willis Robertson and Senator Harry Flood Byrd were among those who voted against this plan.

You would perhaps be interested in knowing that in addition to voting for the resolution which prevented the President of the United States from putting his proposed Reorganization Plan No. 1, into effect, Senator A. Willis Robertson discussed with his colleagues testimony which had been presented before the committee, pointing out that no material economies would result from it and that it was not in accordance with the recommendations of the Hoover Commission. In addition, he voted against the plan as a member of the Committee on Expenditures in the Executive Departments, as well as on the floor of the Senate, when it came up for final action.

Perhaps no one will make a better suggestion than that our membership take the time out for a personal note to Senator Robertson and Senator Byrd in expression of our gratitude for their stand on this matter.

Press Room.

For the convenience of those wishing to contact the press during the convention at the Chamberlin Hotel, please check with the bulletin board there.

CORRESPONDENCE

The Study of Twins.

TO THE EDITOR:

The study of twins is of great value in providing information concerning the respective importance of hereditary predisposition and environmental influences in disease in man. The results of the use of this method have shown an hereditary predisposition to tuberculosis, diabetes, and tumor formation, and a high, medium or low intelligence quotient.

There is some *a priori* evidence showing an hereditary predisposition for peptic ulcer. Only six cases of the occurrence of peptic ulcer in the one or both of mono- or dizygous twins have been reported in the readily accessible literature. Since twins are born in 1 of 86 births and identical twins in 1 of 344 births and the general incidence of ulcer is from 5 to 10 per cent there should be plenty of material available.

I should like to ask physicians to cooperate in assemblying such material by sending me cases in which (1) one or both twins develop peptic ulcer, (2) the site of the ulcer, (3) the age of onset of ulcer, (4) the type of twins (monovular or diovular), (5) the sex of the twins, (6) the date of birth of the twins, and (7) the number and age of the brothers and sisters and the absence or presence of ulcer in each.

Yours sincerely,

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August 30, 1949

BOOK ANNOUNCEMENTS

Poliomyelitis. Papers and Discussions Presented at the First International Poliomyelitis Conference. Compiled and Edited for the International Poliomyelitis Congress. Philadelphia, J. B. Lippincott Company, 1949. xi-360. Illustrated. Cloth.

Marihuana in Latin America The Threat It Constitutes. By PABLO OSVALDO WOLFF, M.D., Ph.D., M.A., Member of Expert Committee on Habit Forming Drugs of the World Health Organization. Sponsored by Washington Institute of Medicine. The Linacre Press, Inc., Washington, D. C. 1939. Pamphlet of 56 pages. Price $1.50.

Atlas of Obstetric Technic. By PAUL TITUS, M.D., Obstetrician-Gynecologist to the St. Margaret Memorial Hospital, Pittsburgh; Secretary, American Board of Obstetrics and Gynecology. Illustrations by E. M. SHACKELFORD, Formerly Medical Illustrator, John C. Oliver Memorial Research Foundation, St. Margaret Memorial Hospital, Pittsburgh. Second Edition. St. Louis, The C. V. Mosby Company. 1949. 197 pages. Cloth. Price $7.50.

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EDITORIALS

Claude Bernard (1813-1878)

THE great French physiologist and father of experimental medicine was the *beau ideal* experimenter. He had wonderful dexterity and a beautifully logical mind so that his experiments were perfectly planned to demonstrate the truth. His frequently quoted advice to those undertaking scientific investigation illustrates his own attitude—"Put off your imagination, as you take off your overcoat, when you enter the laboratory. Before the experiment, and between whiles, let your imagination wrap you around; put it right away from you during the experiment itself lest it hinder your observing power." Garrison says "All of Bernard's greatest discoveries were based upon accidently discovered facts, which he used as clues to larger results through his wonderful power of thinking physiologically." Fulton, on the other hand, says that accident played no part in Bernard's experiments. Be that as it may, no one disputes the importance or the greatness of Bernard's discoveries. He clearly and conclusively demonstrated the function of the pancreatic juice. DeGraaf, nearly 200 years previously, had successfully established pancreatic fistulae in dogs but his experiments with the pancreatic secretion were not conclusive. It remained for Bernard to fully establish the importance of the pancreatic juice.

Bernard's work on the glycogenic function of the liver was entirely without precedent. Foster says that the whole story of glycogen lies in Bernard's own writings. He showed that the liver made glycogen and poured it out into the blood stream as an "internal secretion", a term that he coined. He isolated the carbohydrate which he named glycogen. He also showed that puncture of the floor of the fourth ventricle in dogs produced experimental diabetes. By chemical and histological methods he demonstrated the presence of glycogen in various tissues of the body, especially the muscles and the rapidly growing tissues of the embryo. Seldom has so great a discovery been made and carried out to its conclusion single handed and without outside help. Bernard "not only laid the first stone but left a house so nearly finished that other men have been able to add but little."

His third great discovery was the vaso-motor nerves. He was also interested in the physiological effects of poisons and experimented with curare and carbon-monoxide gas, as well as with anesthesia and asphyxia.

Claude Bernard was born on July 12, 1813 in the village of Saint-Julien near Villefranche. He was educated in the local Jesuit school and at the college at Lyons. For economic reasons he left the college before completing the course and took a position in an apothecary shop. In his off hours he wrote a successful comedy that was played but not published. Later, he wrote a more ambitious drama and at the age of 21 he went to Paris to embark on a literary career. Girardin read the manuscript and recognized its merit. Nevertheless, he advised the young man to study medicine as a surer means of making a living. Bernard followed his advice. In his fifth year he came under the influence of Magendie, becoming first his assistant and finally his successor at Magendie's death. Even with such connection his laboratory facilities were meagre, and most of his early and important work was done in odd corners and out of the way places and in private laboratories.

Very little is said of Bernard's private life. He had a wife and two daughters but his wife became estranged, because she resented Bernard's refusal to go into private practice where the monetary returns would have been greater. One of his daughters spent much of her time founding hospitals for dogs and cats with a view of atoning

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for what she considered the crimes of vivisection, which her father had committed. So he was spared the diversions of family life. His pupils were devoted to him. He received every honor France could give him including membership in the French Academy. When he died on February 10, 1878, he was accorded a public funeral, the first man of science to be so honored.

EDITOR'S NOTE: This is the sixth of a series, "Doctors for whom the public should be thankful."

Rochester, Minnesota

IN 1854 Rochester was a crossroads camp ground in Southern Minnesota for immigrant wagon trains. It was established by George Head of Rochester, New York. At the end of the Civil War it was a country village with nothing to distinguish it from any other county seat in the State. It was unheard of outside of the State of Minnesota. It had however something no other village had. It had a country doctor who had two sons who were fired with the determination of being the best doctors in the world, and with capacities for work that amounted to genius. There were no other medical assets—no healing springs, no salubrious climate. In fact, its first hospital was the direct result of a death-dealing tornado.

At present all the world knows of Rochester and not an inconsiderable part of the people of the world has been there. The benches in the parks and on the sidewalks outside of its hotels are filled with cripples and invalids of all sorts, such as one sees at Excelsior Springs, Missouri, Hot Springs, Arkansas, or the recreation center of Daytona, Florida, in February. According to the *American Guide Series for Minnesota* (1938), Rochester has forty hotels, eighty-four apartment buildings, two hundred rooming houses, twenty restaurants and a twenty acre tourist camp. When an individual starts across the street, either on foot or in a wheel chair, all automobiles stop at a respectful distance as if to say the town is yours, take your time.

St. Mary's Hospital, which was started as a poorly equipped forty bed hospital in 1889 after the tornado, is now one of the great hospitals of the world. Besides, there are two other hospitals and one hotel-hospital with a total capacity of 1533 patients.

Rochester also has the largest pea cannery in the world, but few have ever heard of it. The focal point is the Mayo clinic building, a fifteen story office building with all the latest facilities for prompt and accurate diagnosis. The personnel consists of five hundred staff members and some three hundred and fifty research fellows, together with technicians, nurses, secretaries etc. In the summer some 10,000 patients "go through" the Clinic each month. In the winter months the number drops to 5,000 or 6,000. The greatest number in any one month has been 13,000. This overtaxed the laboratories and they got behind in their reports.

In the park in front of the Clinic is the Mayo Foundation of Hygiene and Medicine which contains a number of models and charts of medical interest. To our mind the most interesting exhibit is an old Bausch and Lomb microscope that has a card describing it as follows: "Bausch and Lomb microscope property of Dr. William Worrall Mayo. It was bought with money obtained from placing a mortgage on the old homestead which occupied the site upon which the Mayo Clinic Building now stands." Such was the beginning of the Mayo Clinic which is present day Rochester. Not only has the Clinic paid its way as it grew, but it has contributed two million dollars to the University of Minnesota as a Foundation for post graduate medical instruction. In this day, when hospitals and medical schools are running in the red and are seeking Federal aid, it is refreshing to know of a medical institution that maintains its independence.

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Never Believe What a Patient Says about Another Doctor

THE Centennial of Sir William Osler's birth was celebrated throughout the world in a remarkable manner. Almost every medical magazine took some notice of it, and some, notably the *Bulletin of the Johns Hopkins Hospital, The Canadian Medical Association Journal* and the *Archives of Internal Medicine* devoted entire issues to reminiscences and sketches of Osler and appraisements of his place in medicine. He was discussed as a clinician, as an investigator, as a pathologist, as a teacher, as a scholar, as a book collector, as a medical historian, as a man and as a promoter of good relations among doctors. His students collected his wise sayings and maxims. They usually went by the name of Oslerisms. One of the most characteristic Oslerism had to do with listening to tales the patient tells about his or her previous doctor. His advice was never to believe what a patient says about another doctor.

Dr. Osler did not qualify this statement. There was no need to. The least reflection would show how unwise it would be to pay any attention to what a patient says on such a subject. In the first place, he or she is a biased and therefore an untrustworthy witness. The patient is either over enthusiastic or else disgruntled. In the second place, an untrained person, especially a sick one, is very apt to misunderstand medical statements. How frequently do your own patients misunderstand your own diagnoses or prognoses? For instance, no wise doctor ever makes a positive diagnosis of early pregnancy even with the newer laboratory tests. It is our invariable rule never to make such a diagnosis and yet we not infrequently hear that we have told a patient positively that she is pregnant. Another statement we frequently hear is that her doctor told her that she could never become pregnant. There is no use to argue about such matters. The best thing to do is to follow Osler's advice and ignore them. It promotes better feeling among doctors.

Tap Water Sodium in the Low Salt Diets

LOW salt diets are being used more and more extensively in the treatment of heart failure, hypertension, renal disease and toxemias of pregnancy. Cole (*J.A.M.A.* **140**:19, 1949) calls attention to the importance of knowing the salt content of the water used in preparing these diets. Where the salt content of the drinking water amounts to more than 10 mgm. per 100 cc. as it does in Aberdeen, S. D., Biloxi, Miss., Crandall, Galveston and Houston, Texas; Galesburg, Ill.; Kansas City and Nevado, Mo.; Los Angeles; Marion, Ohio; Minot, N. D.; Oklahoma City, and Phoenix, Arizona, it seriously interferes with this type of treatment. The problem is further complicated by attempts at softening naturally hard waters. The usual softening process raises the sodium content of the water.

The ordinary routine analysis of public water supplies does not give any information on the sodium content. Sometimes the combined sodium and potassium content is given, but of course that does not help when one is figuring on the sodium content of a diet. Being interested in this subject we asked Dr. Eller, former Health Director of the City of Richmond, about the sodium content of the city's water. He had a special analysis run which shows a sodium content of 5.01 per million which is a negligible quantity.

Charles Armistead Blanton, M.D., LL.D.,

1859-1949

DR. CHARLES A. BLANTON was born in "West Hill", Cumberland County, July 23, 1859 and died at his home, 826 West Franklin Street, September 6th, 1949. While not the oldest member of the Medical Society of Virginia, he had been a member longer than anyone else, having joined the Society in 1881. Dr. Blanton was the son of a doctor and the father and grandfather of doctors, and exemplified all that was finest in the art of medicine.

Graduating at the Medical College of Virginia in 1881, he spent his entire professional life in Richmond. He always enjoyed a fine practice. We say enjoyed advisedly for no one was more complacent with the average patient and no one worked harder over a seriously ill one. In 1887 he became a member of the adjunct faculty of the Medical College of Virginia, which at that time and for a number of years afterwards, was a delightful medical club. In 1894 he was promoted to the faculty, filling the Chair of Materia Medica and Therapeutics until 1898, and the Chair of Children's Diseases until he was made emeritus professor in 1911. It was the contacts with such teachers as Dr. Blanton, who made their living practicing medicine and who of necessity must be masters of the art of medicine as contrasted to the science of medicine, that was such a valuable part of the medical teaching of forty or fifty years ago.

Not only was Dr. Blanton a good doctor but he was also a good citizen and a good churchman. He was a member of the Board of Visitors of Hampden-Sydney College, a member of the finance committee of the Union Theological Seminary, a member of the Society of Colonial Wars and of The Virginia Historical Society. He was a Pi Mu and an O.D.K. He had been a deacon and an elder in the First Presbyterian Church in Richmond, and was an elder of Brown's Presbyterian Church in Cumberland County, a church that was founded by his grandfather, Dr. Jesse S. Armistead. In 1888, Dr. Blanton married Miss Elizabeth Brown Wallace of Fredericksburg. He is survived by one daughter, two sons, Drs. Wyndham B. Blanton and H. Wallace Blanton, five grandchildren and nine great-grandchildren.

Dr. Blanton was always courteous and dignified and was an excellent example to the younger members of our Society.

Floral Eponym

Stapelia

STAPELIUS, JOHANNES BODAEUS D. 1636

STAPELIUS graduated in medicine at Leyden on May 3, 1625, and established himself as a practitioner in Amsterdam. He is said to have been a learned young man with a wide knowledge of Latin and Greek, and a special devotion to botany.

The genus Stapelia of the milk weed family honors him. Stapelia are South African, cactus-like desert plants. The flowers are large and have an unpleasant odor; hence the common name, carrion flower.

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SOCIETIES

Augusta County Medical Association.

At the meeting of this Association held on August 3rd, the following officers were elected: President, Dr. Charles F. Gaylord, Staunton; vice-presidents, Drs. S. G. Saunders, Waynesboro, McKelden Smith, Staunton, and George B. Tyler, Staunton; secretary, Dr. Paul A. Woods, Waynesboro; treasurer, Dr. Boyd H. Payne, Staunton; and censor, Dr. A. F. Robertson, Staunton.

Medical Society of Northern Virginia.

Dr. Amos Koontz, assistant professor of surgery at Johns Hopkins University, Baltimore, was guest speaker at a meeting of this Society on August 9th at Luray. His subjects were "Experiences in Two World Wars" and "Tantalum Mesh in Hernia". Drs. J. A. Miller and G. H. Murphy gave reports of case studies and Dr. M. J. W. White showed a motion picture on leprosy. Dr. H. W. Miller gave a report of the meeting of the Virginia Pharmaceutical Association.

Dr. H. W. Miller, Woodstock, is president of this Society and Dr. F. D. Maphis, Strasburg, secretary.

Orange County Medical Society.

At its meeting on August 17th, Dr. H. C. McCoy, Gordonsville, was elected president to succeed Dr. C. Cameron Kress, Orange; Dr. Frank G. Scott, Orange, vice-president; and Dr. J. Garnett Bruce, Jr., Gordonsville, secretary-treasurer.

Rockingham County Medical Society.

Officers of this society are: President, Dr. Charles C. Powel, Harrisonburg; vice-president, Dr. Hollen G. Helbert, Harrisonburg; and secretary-treasurer, Dr. George S. Row, Bridgewater.

Southampton County Medical Society.

New officers of this Society are: President, Dr. T. A. Morgan (re-elected); vice-president, Dr. Henry R. Gardner, Jr.; and secretary, Dr. W. D. Varner. All are of Franklin.

The Williamsburg-James City County Medical Society

Held its regular bi-monthly meeting in the Library of the Eastern State Hospital preceded by dinner in the Officers Dining Room of the Hospital, the President, Dr. Joseph E. Barrett, presiding. Guests present were Dr. Ralph M. Chambers of New York and Dr. George B. McMurray of Bradenton, Florida, Inspectors from the Central Inspection Board of the American Psychiatric Association, who were engaged in making an inspection survey of the Eastern State Hospital. Another guest was Dr. J. R. Turnage of Sandston. Action was taken by the Society on the death of Dr. Albert M. Sneed, who was the first President of the revived County Society. Under miscellaneous business, Dr. Granville L. Jones, Chairman of the Red Cross Blood Program Committee of the James City County Red Cross Chapter, announced the visit of the Mobile Blood Unit to Williamsburg on October 14th and asked for support and cooperation from the Society.

The scientific session consisted of talks by Mr. W. R. Reese, Clinical Psychologist and Dr. Eleanor Beamer-Maxwell, Acting Psychiatrist, both of the Williamsburg Area Guidance Clinic which is opening at this time. The speakers discussed the general policies and operating procedures of the Clinic. They stressed the need for close cooperation with the Medical Society, asked for reports covering physical factors and history on cases referred by physicians or who had been known by the physicians although the referral was made by the school or some other organization. It was brought out that the Clinic expects to refer back to the family doctor every possible case for treatments which can be rendered by the family doctor. While the Clinic will admit adults, the most hopeful field of work in Mental Hygiene is among children. In some instances in which the child is the referred patient, it will be found helpful or even necessary to treat the parents as well. The Clinic is one being established by the Department of Mental Hygiene and Hospitals of the Commonwealth of Virginia in cooperation with the United States Public Health Service.

GRANVILLE L. JONES,
Secretary-Treasurer

The Smyth County Medical Society

Held its regular meeting at Hotel Lincoln, Marion, on August 17th. This was preceded by a delightful cocktail party given at the home of Dr. and Mrs. D. C. Boatwright, which was attended by twenty-nine including the ladies.

It was moved and seconded that the business be postponed until the next meeting, and members and guests were delightfully entertained by "Dr." Bob Kent, of radio station W.M.E.V., who gave us a talk on "Chiropracty".

RICHARD C. POTTER,
Secretary-Treasurer

Wythe-Bland Medical Society.

Members of the Wythe-Bland Medical Society, meeting on August 26 at the George Wythe Hotel, went on record as being unanimously in favor of voluntary health insurance and opposed compulsory federal health insurance. Every doctor present felt that the greatest service to his patients at the least cost could be rendered through several of the voluntary health insurance plans.

The guest speakers were Dr. W. W. Walton, who spoke on "The Treatment of Burns", and Dr. James Chitwood, who spoke on "Thyroid Diseases". Both speakers are on the staff of the Pulaski Hospital.

The Wythe-Bland Medical Society was reorganized November 1948 and has been holding regular monthly meetings since that time. The President is Dr. C. D. Moore, of Wytheville, Vice-president, Dr. George Kegley, of Bland, and Secretary-Treasurer, J. E. Mangus of Wytheville.

J. E. MANGUS

NEWS

Medical Society of Virginia.

Last call for the 102nd meeting of the Society has been sent all members in the form of the program. The scientific part has been arranged to give something of special interest in each session, and the exhibits—scientific and technical—are up to a high standard. Tuesday evening has been given over to social features. There are many places of special interest to be seen in the vicinity of our meeting place—Fort Monroe—and a large attendance is expected.

The Virginia Diabetes Association

Is having its first meeting at the Hotel Chamberlin at Old Point Comfort, in connection with the Medical Society of Virginia annual meeting, at 3:00 P. M. on Sunday, October 9.

The weather and the place should combine to make a very enjoyable meeting. All members of the state society are invited to attend and any who are interested are urged to join the society. The meeting should be interesting, with papers by different clinicians in the state. Following the scientific program there will be a short meeting for adoption of by-laws and election of officers.

M. C. V. Alumni Dinner.

Medical alumni of the Medical College of Virginia will hold their annual dinner, preceded by a social hour, during the convention of the Medical Society of Virginia at the Hotel Chamberlin, on Monday, October 10 at 5:30 P. M. Dr. Edward L. Alexander will be in charge of the social hour and will preside over the dinner and brief meeting following.

Dr. Harvey B. Haag, Dean of the School of Medicine of the College, will speak on "Trends in Medical Education at the College".

Dr. Waverly R. Payne, Chairman of the Committee on Arrangements for the Society's Convention, will extend greetings from Tidewater Virginia, and Dr. H. Hudnall Ware, Jr., Professor of Obstetrics at MCV, will speak briefly on the War Memorial Alumni Building, the Alumni Association's House, which is now undergoing extensive renovations and which it is hoped will be ready for occupancy before the end of the current year. Dr. Roshier W. Miller, Emeritus Professor of Materia Medica and Therapeutics, will give the invocation.

All alumni of the Medical College of Virginia are urged to attend this dinner and to bring their wives and other guests.

News from the State Department of Health.

Carroll and Grayson counties have a newly established Health Department with Dr. Mildred Esther Scott as Health Officer. Dr. Scott's appointment became effective August 1, 1949.

Dr. Stuart T. Bray has been appointed Health Officer for Buchanan and Tazewell counties, as of October 3, 1949.

Dr. William B. Wild has been appointed Health Officer for the Rockingham-Harrisonburg Health

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District, this appointment becoming effective October 3, 1949.

Dr. S. S. Shouse, Health Officer for Appomattox, Buckingham and Cumberland counties has been granted a year's military leave, effective August 26, 1949.

Dr. W. R. Southward has been appointed Director of Venereal Disease Bureau of the Virginia State Health Department. Dr. Southward begins this work October 1, 1949.

Roanoke City Board of Health.

Dr. E. G. Gill has recently been elected chairman of the Board and Dr. W. R. Whitman, vice-chairman. This is for a two-year period.

Dr. J. D. Middlemas,

Recently of Orange, is now at the University of Virginia Hospital where he is taking a residency in psychiatry.

Post-Graduate Course in Ophthalmology and Otolaryngology.

The Post-Graduate course sponsored by the Virginia Society of Ophthalmology and Otolaryngology will be held November 29, and 30 and December 1 and 2. The first two days are for otolaryngology and the remaining two for ophthalmology. The courses will be given at Baruch Auditorium, Medical College of Virginia, Richmond.

The West Virgina State Medical Association,

At its recent meeting at White Sulphur Springs, elected Dr. Russell B. Bailey of Wheeling as president to assume office January 1, 1950. Dr. T. M. Barber of Charleston was re-elected secretary-treasurer for his twenty-third consecutive term. The 1950 annual meeting will also be held at White Sulphur Springs.

Dr. Breyfogle Resigns.

Dr. Herbert S. Breyfogle, Virginia's first chief medical examiner, has resigned effective October 1st. He will be succeeded by Dr. Geoffrey T. Mann, his assistant, who has been appointed for a three year term beginning October. Dr. Breyfogle advised that he plans to study law on the West Coast.

Dr. Julien H. Meyer,

Roanoke, announces the change of his office to the Shenandoah Building where his practice will be limited to obstetrics and gynecology, including female urology.

Dr. E. B. J. Whitmore,

Recently junior physician at Western State Hospital at Staunton, has been transferred to the post of senior physician at Central State Hospital, Petersburg.

Dr. E. G. Gill,

Roanoke, has returned from Europe where he attended the Fourth International Congress of Otolaryngology. The sessions were held at London, Oxford, Cambridge and Edinburgh. Dr. Gill presented a paper on "The Effects of Air Pollution on the Respiratory Tract".

Dr. O. L. Ramsey, Jr.,

Recently a staff member of the hospital at Holden, W. Va., has opened offices at Madison Heights, Virginia, for general practice.

Dr. Walter E. Vest,

Huntington, W. Va. was elected president of the new West Virginia medical licensing board at its organization meeting this summer.

The Piedmont Proctologic Society,

A sub-section of the American Proctologic Society, was organized in Asheville, N. C. on July 30, 1949. All of the proctologists, who are members of the American Proctologic Society, in the states of Virginia, North Carolina, South Carolina, Tennessee and Georgia are eligible for membership and all of the states were represented at the organization meeting.

Dr. Isaac E. Harris, of Durham, was chairman of the organization committee; Dr. C. S. Drummond, of Winston-Salem, Secretary; Dr. Geo. F. Parker, of Asheville, the host; Dr. W. T. Brockman, of Greenville, was to select a name; Dr. C. R. Deeds, of Hendersonville, to draw up the Constitution and By-Laws.

Dr. W. T. Brockman, of Greenville, S. C. was elected first President; Dr. C. R. Deeds, of Hendersonville, N. C. its first Vice-President; Dr. C. S. Drummond of Winston-Salem, N. C. the first Secretary-Treasurer.

The next meeting will be held in Atlanta, Ga. on December 5, 1949.

Post-Graduate Course on Urinary Tract Disorders.

On November 17, 18, and 19 the Frank E. Bunts Institute and the Cleveland Clinic will present a continuation course for physicians on "Medical and Surgical Disorders of the Urinary Tract". Dr. Herman L. Kretschmer of Chicago will give the evening address November 17 on "Clinical Significance of Hematuria". The other out-of-town guest speaker will be Dr. Louis Leiter of New York, who will speak on "Uremia" Saturday morning, November 19, and who will take part in the panel discussion closing the course.

Inquiries regarding the complete program and registration can be addressed to the Director of Education, Frank E. Bunts Educational Institute, 2020 East Ninety-third Street, Cleveland 6, Ohio.

Post-Graduate Courses in Diseases of the Chest,

Sponsored by the Council on Post-Graduate Medical Education and the New York State Chapter of the American College of Chest Physicians, will be given November 14-18, at the Hotel New Yorker, New York City. Full information may be received from Dr. Frank R. Ferlaino, secretary, 580 Park Avenue, New York 21, N. Y.

Dr. James L. Patterson,

Logan, W. Va. was elected president of the West Virginia Chapter, Medical College of Virginia Alumni Association at its recent meeting.

Jefferson Medical College, Philadelphia,

Has received official word that Dr. A. J. Orenstein of the class of 1905 has been elected an Honorary Fellow of the Royal Society of Tropical Medicine and Hygiene. This honor has been conferred upon only thirty-five men during the forty-two years of the Society's existence. Seven of these men, now deceased, were Americans. There are only seven Honorary Fellows living today, including Dr. Orenstein, the only American.

General Surgeon.

Board eligible; seven years formal training; two years army surgery; desires association with established surgeon, group or private practice opportunity. Married, 39, immediate availability. Write "Surgeon", care the Virginia Medical Monthly, 1200 East Clay Street, Richmond 19. (*Adv.*)

OBITUARIES

Dr. Charles Armistead Blanton

Prominent and beloved Richmond physician, died September 6th. He was a native of Cumberland County and ninety years of age. Dr. Blanton graduated from the Medical College of Virginia in 1881 and had practiced in Richmond since that time. In 1887 he was appointed to the faculty of the College, where he was professor of materia medica and therapeutics, the first professor of pediatrics, and a demonstrator of anatomy. He had been emeritus professor of children's diseases of the College since 1911. Dr. Blanton had been a trustee of Hampden-Sydney College since 1911 and in 1931 the College conferred on him the honorary degree of LL.D., which was the second time in its history they had honored a member of its board. He was very active in the work of the Presbyterian Church of the State, having served as an Elder and on the finance committee of the Union Theological Seminary. Dr. Blanton had been a member of the Medical Society of Virginia for sixty-two years and was made a Life Member at its 1948 meeting. A daughter and two sons, Drs. Wyndham B. Blanton and H. Wallace Blanton, survive him.

Dr. Talmage Bryan Weatherly,

Well-known Richmond eye, ear, nose and throat specialist, died September 4th following a long illness. He was sixty-one years of age and a graduate of the former University College of Medicine, Richmond, in 1912. Dr. Weatherly had practiced in Richmond since 1914 and was at one time ophthalmologist for the Retreat for the Sick Hospital. He was active in many fraternal organizations, among them the Richmond Masonic Lodge. He had been a member of the Medical Society of Virginia for thirty-four years. His wife survives him.

Dr. George Gilbert Crawford,

Prominent physician of Strasburg, died September 6th after an illness of several months. He was seventy-three years of age and a graduate in medicine from the University of Virginia in 1901. Dr. Crawford had practiced at Strasburg for forty-one years and served as its Mayor for twenty years. He

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was president of the Shenandoah Valley Medical Society and a past president of the Medical Society of Northern Virginia. He had been a member of the Medical Society of Virginia for twenty-five years. His wife and five children survive him.

Dr. Henry Garnett Plaster,

Washington, D. C., died August 3rd, having been in ill health for more than a year. He was a native of Bluemont and seventy years of age. Dr. Plaster graduated from the former University College of Medicine, Richmond, in 1899 and practiced in Loudoun County for more than twenty years before locating in Washington in 1925. He had been a member of the Medical Society of Virginia for fifty years and would have been made a Life Member at the annual meeting in October. His wife and two children survive him.

Dr. John William Freed,

Staunton, died June 2nd at the age of seventy-four. He received his medical degree from the University of Virginia in 1901, and was on the staff of the Western State Hospital for forty years. He had been a member of the Medical Society of Virginia for forty-seven years. His wife and three children survive him.

Resolution Upon the Death of Dr. Staige Davis Blackford.

Dr. Staige Davis Blackford died of coronary thrombosis in Charlottesville, Va., July 17, 1949. He was Professor of the Practice of Medicine at the University of Virginia Medical School.

Dr. Blackford was the son of Dr. Launcelot M. Blackford and Eliza Ambler Blackford. He was born December 28, 1898, at Alexandria where his father was headmaster of the Episcopal High School for many years. He attended Episcopal High School and the University of Virginia. He received B.S. and M.D. degrees, the latter in 1925. As a student he was an active leader in all aspects of undergraduate life in school and the university.

Following graduation, he interned at the Massachusetts General Hospital in Boston. He returned to the University of Virginia as a member of the Faculty in 1927. He was the author of numerous articles on tularemia, gall bladder disease, spontaneous pneumothorax, and other topics. He was keenly interested in both under-graduate and post-graduate medical education. As Chairman of the Medical School Committee on Post-Graduate Education, he organized many refresher courses for practicing physicians. He was the first Editor of the University's Medical Alumni Bulletin. He was the first chairman of the Clinical Staff of the University Hospital.

He was a member of the Albemarle County Medical Society, Medical Society of Virginia, American Medical Association, American College of Physicians, American Clinical Climatological Association.

During World War I Dr. Blackford served with the University of Virginia section of the Army Ambulance Service. He was decorated with the Croix de Guerre. Soon after this country entered World War II, he organized the hospital unit, sponsored by the University of Virginia, which became the Eighth Evacuation Hospital. Dr. Blackford served as its Chief of Medicine for more than thirty months in North Africa and Italy. Dr. Blackford was decorated with the Legion of Merit and the Medal of French Morocco. He was released from active duty at the end of the War with the rank of Colonel.

In August, 1927, he married Miss Lydia Fishburn who survives. His son, Staige D. Blackford, Jr., is a student at the University of Virginia. His daughter, Linda Harper Blackford, is a student at St. Anne's School.

As an educator and as a soldier in two wars, his contributions to the University, the State, and the Country he loved, were outstanding. But more remarkable than his tangible accomplishments was his unique personality. His unusual charm, wit, and searching mind, made him a peerless companion. His frankness and intellectual honesty made him a valued critic. His wide vision made him a trusted counsellor. His humanity, kindness, and unusual personal magnetism endeared him to many. Certainly, few people have been considered a "best friend" by so many. To them his untimely death has brought a feeling of genuine sorrow and irreplaceable personal loss.

Offered by the Committee for the minutes of the Albemarle Medical Society:

OSCAR SWINEFORD, JR.
BYRD S. LEAVELL
H. B. MULHOLLAND
J. B. TWYMAN

Resolutions on Dr. Hill.

At a meeting of the Petersburg Medical Faculty held August 8th, the following resolutions were unanimously adopted:

WHEREAS it has pleased our Heavenly Father in His infinite wisdom to remove from our midst our friend and co-worker, Dr. Phillip L. Hill,

BE IT RESOLVED: First, that we deeply appreciated Dr. Hill as a man, citizen and physician; Second, that we deeply deplore our loss; Third, that we extend our sympathy to his family; and Fourth, that a copy of these resolutions be published in the VIRGINIA MEDICAL MONTHLY, the public press of Richmond and the *Progress-Index*, also a copy to be spread on the minutes of the Petersburg Medical Faculty.

J. BOLLING JONES
CLAIBORNE T. JONES
FRANCIS N. TAYLOR